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TREATMENT OF PNEUMONIA IN CHILDREN WITH A SINGLE DOSE OF SULFAPYRIDINE

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The effectiveness of sulfapyridine in the treatment of pneumococcic infections has now been accepted generally. There still remains the problem of determining the best method of administration.

Since the introduction of sulfapyridine for the treatment of pneumonia in children the recommended duration of treatment has steadily decreased, and the estimates of effective levels in the blood have been revised downward. At present the commonly accepted daily dosage is approximately 0.2 Gm. per kilogram of body weight, in divided doses, and the drug is usually given for from two to four days. A level of 4 mg. of free sulfapyridine per hundred cubic centimeters of blood has been accepted as satisfactory, and favorable therapeutic results have been obtained with levels as low as 2 mg. per hundred cubic centimeters.[1] The experimental work of Long and Feinstone [2] has shown that the excretion of sulfapyridine is slower than that of sulfanilamide.

It was decided to determine the levels in the blood and to evaluate the clinical results following the administration of one large dose of sulfapyridine, to see whether effective levels in the blood, maintained long enough to produce a cure, would result.

During the winter of 1939-1940 all patients admitted to the wards of the Children's Hospital with pneumonia received only one dose of sulfapyridine. Private patients continued to be treated by the multiple dose method in varying doses. In the series studied there were 41 patients, ranging in age from 2 months to 12 years. Six children were less than 6 months old, and a total of 15 children (37 per cent) were under 1 year of age.

The roentgenologic diagnosis was lobar pneumonia in 27 cases and bronchopneumonia in 14 cases. In several cases roentgen findings first

From the Children's Hospital, Buffalo.

1. Cullen, G. E., in Round Table Discussion of Treatment of Pneumonia in Infants and Children, J. Pediat. **16**:254, 1940.

2. Long, P. H., and Feinstone, W. H.: Observations upon the Absorption and Excretion of Sulfapyridine, Proc. Soc. Exper. Biol. & Med. **39**:486, 1938.

became positive several days after sulfapyridine was given, when the patients were afebrile and much improved clinically.

In each case nasopharyngeal and gag cultures were made. Pneumococci were recovered in 37 cases. These have been listed according to type (table 1). In 14 instances the pneumococci were associated with hemolytic streptococci, in 3 cases with influenza bacilli and in 1 case with both these organisms. In 2 cases the cultures yielded only hemolytic streptococci, in 1 case only influenza bacilli and in the remaining case both organisms. Blood cultures were made in 21 instances. One, made post mortem, showed staphylococci. The others were sterile.

In 7 instances the duration of the disease could not be determined. In the remaining 34 cases, 22 patients were treated within three days and 29 within four days after the onset.

DOSE AND MODE OF ADMINISTRATION

The amount of sulfapyridine given was 0.3 Gm. per kilogram of body weight (2 grains per pound), as a suspension in either milk or a formula. With the

TABLE 1.—*Results of Nasopharyngeal and Gag Cultures*

Type of Pneumococcus	Number of Times Recovered
VII	9
XIV; XIX; untyped	4
XII	3
I; V; VIII; VII + VIII	2
III; XI; XXII; XXXII; I + IV	1
Total	37

exception of 2 children who each received 5 Gm., the maximum dose was 4 Gm., which meant that the older children received less than 0.3 Gm. per kilogram (table 2). Although in a few instances considerable coaxing was necessary before the children took this large amount of sulfapyridine, in no case was it necessary to resort to gavage. After administration of the drug nothing was given by mouth for four hours. In 3 instances immediate vomiting necessitated another dose. After four hours the children were given food as desired, and fluids were forced.

THERAPEUTIC RESULTS

In 34 cases the rectal temperature dropped to 100 F. or below within twenty-four hours after the drug was given. A composite curve of rectal temperatures taken every four hours showed that the average temperature was 100 F. or below at all times after twenty hours had elapsed. In 5 cases (2, 4, 5, 9 and 18) the fever continued after forty hours. Four of the 5 patients had levels of 6.9 mg. per hundred cubic centimeters of blood or higher. Two of these 5 patients died. One was an 8 month old child who was acutely ill when admitted and died thirty-six hours later, without responding to therapy. A culture of the blood

taken post mortem showed 50 colonies of Staphylococcus aureus per cubic centimeter. The other patient was a 14 month old child who was spastic and mentally defective; death occurred after three weeks. Autopsy revealed persistence of the pneumonia and widespread thromboses of

TABLE 2.—*Concentrations of Free Sulfapyridine in the Blood Following Single Oral Dose of Sulfapyridine*

Case No.	Age Yr.	Age Mo.	Weight, Kg.	Dose, Gm. per Kg.	Level* in Blood, Mg. per 100 Cc. Hours After Administration 1-3	4-6	7-9	10-15	16-21	22-27	28-33	34-39	40-60
Group 1†													
1	1	8	10.0	0.30	...	7.0	...	7.0	...	10.1	...	3.5	1.9
2		9	8.2	0.30	...	4.5	...	...	8.1	...	4.8	...	1.8
3		3	5.9	0.34	...	...	...	...	4.9	6.4	...	...	...
4		5	5.5	0.29	...	...	9.4	...	7.1	...	2.7	...	Trace
5		6	6.8	0.29	...	...	9.1	...	6.1	...	1.6	...	...
6	3	5	10.9	0.28	7.2	...	8.9	...	6.0	3.9	...	1.5	...
							7.3	...	4.0	1.8	...	...	Trace
7		2	3.6	0.28	...	7.8	...	6.9	5.3	...	3.3	...	...
8	1	1	7.7	0.32	...	6.9	...	...	5.3	...	...	...	...
9‡		8	6.4	0.31	...	...	6.3	...	...	6.3§	...	...	...
10	3	3	13.6	0.29	...	...	6.3	...	3.9	...	1.7	...	...
11		10	6.8	0.29	5.3	...	6.4	...	2.8	1.3	...	...	...
12	1	1	10.0	0.30	...	...	6.2	...	3.8	...	2.0	...	Trace
13		11	11.4	0.35	...	...	...	5.6	4.0	...	...	1.6	...
14	2	2	10.5	0.29	4.4	5.7	5.8	...	3.9	3.2	1.9	1.2	Trace
15	1	2	12.7	0.31	...	...	5.7	...	...	...	...	...	...
16		7	8.6	0.29	...	3.2	...	...	...	1.5	...	...	...
17	2	..	11.4	0.29	...	...	...	...	2.0	...	0.8	...	...
18‡	1	2	6.8	0.29	...	...	2.1	...	Trace	...	...	...	...
Group 2#													
19	3	4	15.9	0.25	2.7	3.5	4.8	...	8.1	10.3	4.9	...	1.7
20	5	1	17.3	0.23	...	...	11.0	...	...	...	3.9	...	...
21	9	4	25.0	0.20	...	...	...	7.2	...	4.7	...	...	...
22	2	3	13.2	0.25	...	7.2	...	...	...	4.5	...	...	1.5
23	5	2	15.0	0.27	5.7	6.8	6.3	...	4.9	...	1.9	...	...
24	7	4	20.5	0.24	...	...	5.4	...	...	...	...	Trace	...
25	7	2	18.6	0.22	...	...	3.8	...	2.4	...	...	...	...
26	7	..	18.6	0.22	...	2.7	3.8	...	Trace	...	...	...	...
Group 3¶													
27	5	5	23.2	0.17	...	...	11.0	...	4.4	...	1.8	...	...
28	9	3	26.4	0.15	...	...	5.2	...	6.8	...	...	...	...
29	8	10	24.1	0.17	...	...	5.3	...	2.3	...	0.8	...	...
30	2	10	12.6	0.15	...	4.4	...	...	...	2.3	...	...	...
31	6	3	21.4	0.19	4.0	...	4.8	...	1.8	1.0	...	...	...
32	11	9	29.5	0.14	2.0	2.8	...	...	2.6	1.6	...	...	...
33	8	10	25.5	0.16	...	...	...	2.5	...	...	...	...	...
34	6	10	24.1	0.17	2.5	...	...	1.9	...	Trace	...	...	...
35		11	9.5	0.16	...	...	1.9	...	...	Trace	...	...	...

* Highest level of each patient is in bold face type.
† Patients receiving between 0.29 and 0.35 Gm. per kilogram of body weight.
‡ Patient died.
§ Blood taken post mortem.
# Patients receiving between 0.2 and 0.28 Gm. per kilogram.
¶ Patients receiving between 0.15 and 0.19 Gm. per kilogram.

the dural sinuses. These were the only 2 deaths in the entire series, giving a mortality rate of 5 per cent.

In 1 case slight hydrothorax developed, which cleared spontaneously. No cases of empyema occurred. One child responded promptly to treatment, but on the fourth day the pneumonia spread to another lobe. He responded promptly to a second single dose of sulfapyridine.

In 14 cases (34 per cent) there was a secondary rise in temperature, usually on the second or third day after administration of the drug, although in 2 cases it occurred as late as the sixth day. With this secondary elevation of temperature the children did not look particularly ill, and in all but 2 cases the temperature was normal within twenty-four hours. Three of these children were given additional sulfapyridine, but the defervescence seemed no more rapid than in the untreated patients. This secondary rise in temperature has been mentioned in previous reports. The cause is unknown, but it does not seem to be important clinically.

COMPLICATING FACTORS

In 1 case pneumonia followed pertussis, and in another the onset of the pneumonia occurred several days after the exanthem of varicella had appeared. In 1 case varicella developed the day following hospitalization for the pneumonia. In 6 cases aural drainage followed either myringotomy or spontaneous rupture. In 3 instances pneumococci were cultured from the aural discharge, and in 2 instances Staph. aureus was recovered. In no case did mastoiditis develop. In 7 other instances infections of the middle ear subsided without drainage.

LEVELS OF SULFAPYRIDINE IN THE BLOOD

The levels of free sulfapyridine were determined in 35 cases by the use of Marshall's [3] method for the determination of sulfanilamide. A standard for sulfapyridine was substituted. In most cases determinations were done at varying intervals (table 2). The cases have been divided into three groups on the basis of the dose received: from 0.29 to 0.35 Gm., from 0.2 to 0.28 Gm. and from 0.15 to 0.19 Gm., per kilogram of body weight. In each group the cases have been listed according to the levels of the drug in the blood.

The levels in the blood tended to be higher and to be maintained over a longer period with the higher doses. However, there was enough overlapping to confirm previous reports of considerable variations in levels in the blood following the same dose of sulfapyridine. One child (case 6) received a second dose of the drug five days after the original dose in treatment for spread of the pneumonia. It is of interest that there was a difference of 2 mg. per hundred cubic centimeters of blood in the levels resulting from the two doses.

In most cases there was a considerable amount of the drug in the blood stream within a few hours after the drug was administered, but the level rose slightly for several more hours. Thereafter, there was a

3. Marshall, E. K., Jr., and Litchfield, J. T., Jr.: The Determination of Sulfanilamide, Science **88**:85, 1938.

fall varying widely in rapidity. In 6 cases the levels continued to rise for as long as eighteen to twenty-seven hours after the drug was given.

In 26 cases levels above 4 mg. per hundred cubic centimeters of blood were obtained, and in most of these instances satisfactory levels were maintained in the blood for at least eighteen hours. In a considerable number of cases effective levels were maintained in the blood for at least thirty hours. In the remaining 9 cases the lowest level was 1.9 mg. per hundred cubic centimeters of blood. In 1 of these cases the child died. In the other 8 the defervescence was as prompt and the clinical course as satisfactory as in the cases in which the level was above 4 mg. per hundred cubic centimeters of blood.

TOXIC EFFECTS

There were surprisingly few toxic effects. In 1 child transient microscopic hematuria developed. No rashes, blood dyscrasias or untoward mental symptoms were noted.

In the forty-eight hours following administration of the drug 21 (50 per cent) of the patients had no emesis, 12 (30 per cent) vomited once and 8 (20 per cent) vomited more than once. In this series most of the vomiting occurred when the children first received fluids, four hours after the drug was given. This vomiting did not interfere with the therapy, because by that time the sulfapyridine had already passed into the intestinal tract and had been largely absorbed. Only 2 children had persistent vomiting, and 1 of these had pertussis. In a recent report on 100 patients treated by the multiple dose method, Christian and his associates [4] stated that 73 per cent vomited at least once and 57 per cent more than once.

COMPARISON WITH CONTROL GROUP

During the period of this study 24 private patients were treated by the multiple dose method. Clinically, these children appeared no sicker than those in the ward. Three were under the age of 6 months, and a total of 6 (25 per cent) were less than 1 year old. Four of these infants died in spite of receiving between 0.8 and 2.0 Gm. of sulfapyridine daily. Levels in the blood were not determined. In this group the duration of treatment varied from one to five days, with an average of two and eight-tenths days. The total number of doses varied between two and twenty-two, with an average of eleven doses for each child. Three children had no emesis, 3 vomited once and 18 more than once. Four children each vomited more than ten times. The average number of emeses was 4.7, compared with an average of 1.1 for the group

4. Christian, H. S.; Jorgensen, G. M., and Ellis, C.: Treatment of Pneumococcic Infections in Children with Sulfapyridine, Am. J. Dis. Child. **59**:1 (Jan.) 1940.

treated with one dose. There were 4 deaths, giving a mortality rate of 16 per cent. It is interesting to note that only 1 child (4 per cent) had a secondary rise in temperature, compared with 34 per cent in the group given a single dose.

COMMENT

In the cases included in this study the single dose method gave satisfactory levels in the blood in most cases, and the clinical results were as good as, if not better than, those in the group that received multiple doses. If the results are as good, it would seem desirable to adopt a single dose method, for the following reasons:

1. It is simpler, interferes less with the child's rest and sleep during the time when he is most ill and is less demanding on the nursing staff.

2. It decreases the incidence of the most common toxic effect, nausea and vomiting.

For the ordinary case of uncomplicated pneumonia it would appear that 0.3 Gm. of sulfapyridine per kilogram of body weight administered in one dose will give satisfactory results. Lower doses are not so consistent in giving levels in the blood above 4 mg. per hundred cubic centimeters. Although the lower levels gave satisfactory results, it would seem safer to use the larger dose. If it is thought desirable to maintain levels in the blood above 4 mg. per hundred cubic centimeters for more than twenty-four hours, the dose can be repeated at eighteen to twenty-four hour intervals. Such repetition is probably advisable when the patient cannot be watched closely and would probably decrease the number of cases in which a secondary rise in temperature occurs.

CONCLUSIONS

After the oral administration of a single dose of 0.3 Gm. of sulfapyridine per kilogram of body weight, the free sulfapyridine in the blood usually reaches levels of at least 4 mg. per hundred cubic centimeters within a few hours. In most cases a considerable concentration persists for at least twenty-four hours.

In some cases the highest levels in the blood occur after twenty-four hours, indicating that absorption from the gastrointestinal tract may continue for that length of time.

The administration of a single dose of sulfapyridine of 0.3 Gm. per kilogram of body weight to children with pneumonia gives satisfactory therapeutic results.

Levels in the blood above 2 mg. per hundred cubic centimeters give satisfactory results in most cases of pneumonia in childhood.

The use of the single dose method simplifies the treatment of pneumonia and decreases the incidence of toxic effects.

ASCORBIC ACID CONTENT OF COW'S MILK AT VARIOUS STAGES OF LACTATION

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In a study of the average ascorbic acid content of milk produced by a mixed dairy herd, Rasmussen, Guerrant, Shaw, Welch and Bechdel [1] found that the ascorbic acid content of milk was "relatively high during the early stages of lactation, but decreased to a minimum after about two months of lactation, and then increased to a maximum in the later stages of lactation." These authors also reported that the ascorbic acid content of milk varies with breeds of cows, being 50 per cent greater for Brown Swiss than for Holstein cows, and it appears from their data that the proportion of milk from cows of each of the five breeds under observation was not uniform for all the mixed milks assayed at the thirteen monthly periods.

Whitnah and Riddell [2] reported that during the first month of lactation milk has about a 10 per cent lower vitamin C content than in later months and that the stage of lactation is one of the "most important factors causing variations in the vitamin C content of fresh milk from well fed cows."

In contrast to these observations, Reedman [3] concluded from the determination of the ascorbic acid content of samples of milk collected in November from four breeds of dairy cows that there was little variation at different stages of lactation.

From the Research Laboratories of the E. L. Patch Co. (A. D. H. and F. T.), H. P. Hood and Sons, Inc. (E. A. W.) and the University of North Carolina (G. H. S.).

1. Rasmussen, R.; Guerrant, N. B.; Shaw, A. O.; Welch, R. C., and Bechdel, S. I.: The Effects of Breed Characteristics and Stages of Lactation on the Vitamin C (Ascorbic Acid) Content of Cow's Milk, J. Nutrition **11**:425-432, 1936.

2. Whitnah, C. H., and Riddell, W. H.: Variations in the Vitamin C Content of Milk, J. Dairy Sc. **20**:9-14, 1937.

3. Reedman, E. J.: The Ascorbic Acid Content of Milk, Canad. Pub. Health J. **28**:339-340, 1937.

In view of the conflicting nature of the published reports and the limited data in the literature consulted, it seemed desirable to accumulate additional data concerning the influence of the stage of lactation on the ascorbic acid content of milk. Accordingly, it was arranged to obtain data on two breeds of cows and to correlate the results separately.

PROCEDURE

The samples of milk used in this investigation were taken at bimonthly intervals throughout a one year experimental period from Guernsey and Holstein cows

TABLE 1.—*Composition of Dairy and Fitting Rations*

Components	Per Cent
Dairy Ration	
Calcium carbonate	0.5
Iodized salt	1.0
Steamed bone meal	1.0
Yellow corn meal	5.0
Soybean oil meal (expeller process)	5.0
Cane molasses	5.0
Corn gluten feed	10.0
Yellow hominy feed	10.0
Distillers' corn grains, dried	10.0
Cottonseed meal, 41% (hydrolic process 5% fat)	10.0
Oats (crimped)	17.5
Wheat bran	25.0
Home-Mixed Fitting Ration	
Steamed bone meal	1.0
Calcium carbonate	1.0
Iodized salt	1.0
Cane molasses	7.0
Yellow corn meal	10.0
Soybean oil meal (expeller process)	10.0
Yellow hominy feed	15.0
Wheat bran	25.0
Oats (crimped)	30.0
Commercial Fitting Ration	
Carotene	Unknown
Iodized salt	Unknown
Calcium carbonate	Unknown
Molasses	Unknown
Dried beet pulp	Unknown
Alfalfa meal	Unknown
Wheat bran	Unknown
Wheat middlings	Unknown
Soybean oil meal	Unknown
Crushed oats	Unknown
Corn gluten meal	Unknown
Corn meal	Unknown

maintained on a Massachusetts certified milk farm under the uniform and carefully controlled conditions described in a previous publication.[4] Since it had been found in an earlier investigation [5] that the age of the cow did not significantly influence

4. Holmes, A. D.; Tripp, F.; Woelffer, E. A., and Satterfield, G. H.: A Study of Breed and Seasonal Variations in the Ascorbic Acid Content of Certified Milk from Guernseys and Holsteins, J. Nutrition **17**:187-198, 1939.

5. Holmes, A. D.; Tripp, F.; Woelffer, E. A., and Satterfield, G. H.: The Influence of the Age of the Cow on the Ascorbic Acid Content of Certified Milk, Food Research **5**:263-273, 1940.

the amount of ascorbic acid in her milk, the samples were taken from cows varying from 3 to 11 years of age, throughout all stages of lactation. Twenty-eight Guernsey and 27 Holstein cows were tested in the course of this investigation.

During the entire experimental period of twelve months, all cows received daily a ration composed of various combinations of the following ingredients: a commercial fitting ration with irradiated yeast; home-mixed fitting ration with irradiated yeast; a dairy ration without yeast; mixed hay, legume and grass silage, and first and second grades of alfalfa hay. The composition of these rations is given in table. 1.

The various components of the rations were assayed for their ascorbic acid content by the method of Tillmans and co-workers [6] as modified by Bessey and King [7] and described by us in a previous publication.[4] The results of these assays are given in table 2.

The experimental cows, which were under supervision of a veterinarian, were housed in modern dairy barns throughout the experimental period. The cows were allowed exercise in open yards but at no time had access to pasture. Since the usual lactation period for dairy cows terminates after from ten to twelve months, only a few cows were available beyond the tenth month of lactation.

TABLE 2.—*Ascorbic Acid Content of the Components of the Experimental Ration*

Components	Mg. of Ascorbic Acid per 100 Gm. of Feed
First grade baled alfalfa	1.883
Commercial fitting ration with irradiated yeast	1.622
Grass silage	1.548
Second grade baled alfalfa	1.380
Good farm hay (one half alfalfa)	1.334
Second grade farm hay (all grass)	0.907
Milking ration with irradiated yeast	0.754
Beet pulp	0.669
Fitting ration and irradiated yeast	0.592
Milking ration	0.562

Samples of morning milk were taken in 30 cc. flint glass bottles and immediately placed on ice out of contact with light. Kon and Watson,[8] Hand, Guthrie and Sharp [9] and Knight, Dutcher and Guerrant [10] found that exposure to light destroys ascorbic acid in milk. Assays of these samples for their ascorbic acid content by the usual indophenol titration method [4] were commenced within six hours after the milk had been taken from the cow. The results of these assays are reported in terms of milligrams of ascorbic acid per thousand cubic centimeters of milk.

6. Tillmans, J.; Hirsch, P., and Jackisch, J.: Reduction Capacity of Plant Foodstuffs and Its Relation to Vitamin C: V. Antiscorbutic Action of Various Extracts of Cucumber, Ztschr. f. Untersuch. d. Lebensmitt. **63**:276-283, 1932.

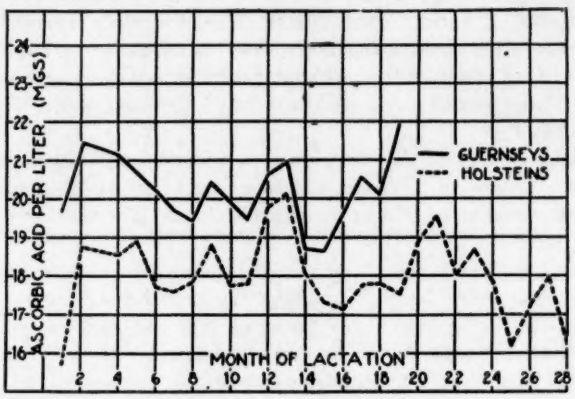
7. Bessey, O. A., and King, C. G.: The Distribution of Vitamin C in Plant and Animal Tissues, and Its Determination, J. Biol. Chem. **103**:687-698, 1933.

8. Kon, S. K., and Watson, M. B.: The Effect of Light on the Vitamin C of Milk, Biochem. J. **30**:2273-2290, 1936.

9. Hand, D. B.; Guthrie, E. S., and Sharp, P. F.: Effect of Oxygen, Light and Lactoflavin on the Oxidation of Vitamin C in Milk, Science **87**:439-441, 1938.

10. Knight, C. A.; Dutcher, R. A., and Guerrant, N. B.: The Quantitative Determination of Vitamin C in Milk, Science **89**:183-185, 1939.

Rasmussen and co-workers [1] and Kon and Watson [11] found that the ascorbic acid content of colostrum was higher than that of the milk produced a few days later. However, since the ascorbic acid content of colostrum is of little significance



Ascorbic acid content of milk from Guernsey and Holstein cows during different months of lactation.

TABLE 3.—*Ascorbic Acid Content of Cow's Milk at Different Stages of Lactation*

Month of Lactation	Guernseys					Holsteins				
	Number of Cows	Number of Tests	Ascorbic Acid, Mg. per 1,000 Cc.			Number of Cows	Number of Tests	Ascorbic Acid, Mg. per 1,000 Cc.		
			Minimum	Maximum	Average			Minimum	Maximum	Average
1	6	9	11.07	24.02	19.69	2	4	14.34	18.17	15.68
2	11	19	16.83	27.00	21.49	10	16	14.34	23.18	18.71
3	18	29	15.37	28.23	21.36	11	21	15.45	22.79	18.63
4	19	33	12.32	25.74	21.20	14	25	15.09	22.62	18.52
5	18	34	16.56	24.30	20.68	16	32	14.30	25.27	18.85
6	18	33	15.22	25.48	20.23	16	30	10.97	24.76	17.62
7	19	35	13.78	23.70	19.68	18	29	14.40	21.08	17.57
8	18	36	14.67	23.65	19.39	19	33	12.35	21.95	17.82
9	16	27	16.86	25.03	20.44	17	31	13.41	23.36	18.84
10	12	18	14.95	24.30	19.95	11	20	9.84	22.14	17.71
11	6	10	15.50	21.82	19.46	8	14	10.70	23.44	17.77
12*	4	10	17.46	23.82	20.63	4	8	14.51	22.84	19.81
13	4	8	17.61	24.08	20.93	4	8	16.35	23.25	20.11
14	3	4	18.51	19.16	18.68	5	9	15.30	21.17	18.07
15	2	3	15.81	20.43	18.64	5	9	13.97	19.36	17.32
16	1	3	18.99	20.03	19.52	5	9	13.50	20.70	17.16
17	1	1	.....	.....	20.57	5	9	13.72	20.58	17.75
18	1	2	19.05	21.26	20.16	6	8	11.50	20.63	17.78
19	1	1	.....	.....	21.95	3	4	13.12	18.87	17.60
20	..	..	.....	.....	.....	1	2	18.21	19.63	18.92
21	..	..	.....	.....	.....	1	2	19.54	19.55	19.55
22	..	..	.....	.....	.....	1	3	16.90	19.70	18.05
23	..	..	.....	.....	.....	1	2	18.28	19.10	18.69
24	..	..	.....	.....	.....	1	1	.....	.....	17.92
25	..	..	.....	.....	.....	1	3	14.43	17.82	16.12
26	..	..	.....	.....	.....	1	2	16.41	18.03	17.22
27	..	..	.....	.....	.....	1	1	.....	.....	17.95
28	..	..	.....	.....	.....	1	2	14.05	18.22	16.14

when considering the food value of commercial milk, the first samples of milk were taken after the colostric period. In table 3 and in the chart are recorded the

11. Kon, S. K., and Watson, M. B.: The Vitamin C Content of Cow's Milk, Biochem. J. **31**:223-226, 1937.

average values of the ascorbic acid content of all samples from each breed of cows assayed during each month of lactation.

Three hundred and fifteen samples of Guernsey milk, representing milk produced by cows in the first to the nineteenth months of lactation, were assayed for their ascorbic acid content. Two hundred and eighty-four samples, or about 90 per cent of the total, were obtained from cows in from the second to the twelfth month of lactation, or the period of lactation typical of the cows in an average commercial dairy.

Three hundred and thirty-seven samples of Holstein milk were assayed for their ascorbic acid content. While these samples represented milk produced by cows in from the first to the twenty-eighth month of lactation, approximately 75 per cent of them were of milk produced during the second to eleventh months inclusive.

RESULTS

The lowest value for ascorbic acid obtained for Guernsey milk was 11.07 mg., which was in milk produced during the first month of lactation. The highest value, 28.23 mg., was in milk produced during the third month of lactation. The average monthly values varied from 18.64 mg. per thousand cubic centimeters, in milk produced by 2 cows in the fifteenth month of lactation, to 21.95 mg., in the milk of 2 cows in the nineteenth month of lactation. The lowest and highest average values obtained during the ordinary commercial lactation period were 19.39 mg. per thousand cubic centimeters, in milk produced by 18 cows in the eighth month of lactation, and 21.49 mg., in milk produced by 11 cows in the second month of lactation. Thus the ascorbic acid content of the Guernsey milk varied from month to month but decreased slightly over the period from the second to the eleventh month of lactation, which is the length of lactation customary in the commercial dairy.

The lowest amount of ascorbic acid found in Holstein milk was 9.84 mg., which was in milk produced in the tenth month of lactation. The highest amount, 25.27 mg., was present in milk produced in the fifth month of lactation. The average monthly values for ascorbic acid in the Holstein milk varied from 15.68 mg. per thousand cubic centimeters, in the milk of 2 cows in the first month of lactation, to 20.11 mg., in the milk of 4 cows in the thirteenth month of lactation. However, the variation in the average monthly values for ascorbic acid during the stages of lactation typical of the average commercial dairy was from 15.68 mg., in milk produced during the first month of lactation, to 18.85 mg., in milk produced during the fifth month of lactation. The average amount of ascorbic acid in the Holstein milk produced during the second to the fifth months of lactation was quite uniform. The ascorbic acid content of the Holstein milk produced during the sixth, seventh, eighth, tenth and eleventh months of lactation was uniform but definitely less uniform than that of milk produced in the second to fifth months inclusive.

The ascorbic acid content of milk produced during the twentieth to the twenty-eighth months of lactation inclusive was determined from a

single cow's milk. While this cow's milk decreased in ascorbic acid content from the twentieth to the twenty-eighth month of lactation, it is interesting that even at the close of this excessively long lactation period, the ascorbic acid content of her milk was as high as for some others of the same breed at the beginning of their lactation periods.

In connection with the variation of the ascorbic acid content of cow's milk at different stages of lactation, it is interesting to note that Harris and Ray [12] found the vitamin C content of human milk at different stages of lactation was: at two months, 60 mg. per thousand cubic centimeters; at three months, 58 mg.; at four months, 40 mg.; at five months, 60 mg.; at eight months, 60 mg., and at ten months, 51 mg.

SUMMARY

The ascorbic acid content of both the Guernsey and the Holstein milk rose rapidly during the first two months of lactation. The amount of ascorbic acid in the milk of both the Guernseys and the Holsteins decreased from the second to the eleventh month of lactation. The data which were assembled for milk produced from the eleventh to the nineteenth month of lactation for the Guernseys and from the eleventh to the twenty-eighth month of lactation for the Holsteins are of considerable interest but are of little practical importance, since the average commercial dairy would contain few cows beyond the eleventh month of lactation.

The least ascorbic acid in the Guernsey milk was 11.07 mg., which was in milk produced during the first month of lactation, and the greatest was 28.23 mg., which was in milk produced during the third month of lactation. The average monthly values for ascorbic acid in Guernsey milk during the first ten months of lactation varied from 19.39 mg. per thousand cubic centimeters for the eighth month to 21.49 mg. for the second month.

The least ascorbic acid in the Holstein milk was 9.84 mg., which was in milk produced during the tenth month of lactation, and the greatest was 25.27 mg., which was in milk produced during the fifth month of lactation. The average monthly values for ascorbic acid in Holstein milk during the first ten months of lactation varied from 15.68 mg. per thousand cubic centimeters for the first month of lactation to 18.85 mg. for the fifth month.

The ascorbic acid content of both Guernsey and Holstein milk decreased slightly over the period from the second month to the eleventh month of lactation, which represents the period of lactation during which commercial milk is usually produced.

Mr. A. A. Colley and Mr. E. C. Steele gave assistance during this study.

12. Harris, L. J., and Ray, S. N.: Diagnosis of Vitamin-C Subnutrition by Urine Analysis, Lancet **1**:71-77, 1935.

NEUROMUSCULAR MECHANISM OF THE INFANT

DEVELOPMENT REFLECTED BY POSTURAL ADJUSTMENTS TO AN INVERTED POSITION

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When an infant is held up by the feet in an inverted position definite attempts to adjust to the unusual situation can be observed. The features which characterize the adjustment exhibit regular sequential change as age advances. The situation is simple and the response is relatively uncomplicated; probably for this reason it has been unusually informative in reflecting maturation of the neuromuscular mechanism.

The present study of postural adjustment to an inverted position has been made in a group of 77 children over a period of approximately five years. Observations were made at weekly or less frequent intervals; the total number of observations was 2,841. Of these 1,382 were recorded on motion picture film, and 1,459 consisted of written protocols. Approximately 7,500 feet of film were exposed in making the records. In addition to the data for the group, daily records (four or five days a week) were obtained on 4 additional infants during the first twelve or eighteen months of life for the purpose of accumulating longitudinal data on the same activity.

Analysis of the records was carried out along lines similar to those which have been used in the study of other behavior patterns; that is, those features were sought which in a broad way appeared to reflect advancement in organization within the nervous system, and, in order not to cloud the issue, little attention was paid to individual peculiarities. With this purpose in mind four distinct phases in the postural adjustment were selected; the features characterizing these phases are portrayed by the line drawings of figure 1. Subsequently, each of the 2,841 individual records was examined and allocated to that phase which most accurately represented the stage of development described in the record. The phase of allocation was checked with a plus rating and the other three phases with minus ratings. The basis of the ratings will be clarified by the following detailed description of the identifying features of each phase.

From the Normal Child Development Study of the Department of Pediatrics, College of Physicians and Surgeons, Columbia University, and the Babies' Hospital.

CRITERIA USED IN RATING POSTURAL ADJUSTMENT TO INVERSION

A. Newborn or Flexor Phase.—At the time of birth the predominance of the flexor muscles is clearly evident. In the inverted position the infant makes an effort to maintain the position of flexion against the pull of gravity. The lower extremities are usually flexed at the two major foci, the knees and the hips; the upper extremities are flexed and adducted on the chest. If the effect of gravity is such that the infant cannot maintain a satisfactory degree of flexion, the effort to do so is indicated by an up and down movement of the body as a result of the tension and release of the flexor muscles in the lower extremities. There is often considerable torsion in the muscles of the trunk. Crying is a frequent concomitant of the activity at this stage. The characteristic posture of the newborn phase is represented by *A*

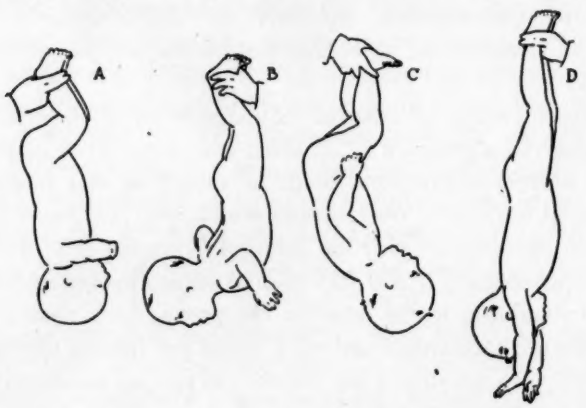

Fig. 1.—Drawings illustrating four phases of postural adjustment to a position of suspended inversion. (From McGraw, M. B.: Growth: A Study of Johnny and Jimmy, New York, D. Appleton-Century Company, Inc., 1935.)

of figure 1. A plus rating was assigned to this phase whenever the baby maintained the flexed posture or made an effort to do so.

B. Extensor Phase.—After the first four or six weeks of life the development of extensor musculature becomes evident. In the inverted position the inception of extensor development is manifested by fleeting extensor movements in the cervical portion of the spine. Within another few weeks the tendency toward extension advances caudad until it embraces the entire vertebral column. At the maximum of the extensor phase the characteristic posture shows an arching of the spinal column, as illustrated by *B* of figure 1. The development of the extensor muscles is not restricted to the trunk but is also noted in the extremities. The arms usually are held in extension and abduction; there is appreciably less flexion than in phase A at the joints of

hip and knee. Crying at this stage is infrequent. During the transition from phase A to phase B there may be occasions when neither flexion nor extension is marked, or, in other instances, the baby may show the flexed posture of the newborn period for a brief moment, then follow it by some degree of spinal extension. Such instances have been rated plus in both phase A and phase B in order to show the overlapping or gradual transition from one phase to another.

C. Righting Phase.—Within a few more months the baby begins to show awareness of the inverted position. This phase also is characterized by flexion, albeit the flexion is of a deliberate quality, quite different from that of the newborn period. Flexion is most marked at the pelvis, so that the shoulder girdle is held in a plane slightly anterior to the pelvic girdle; the neck is flexed, bringing the head forward with the chin toward the chest. There is usually considerable emotional arousal. The child may seize his own thighs, reach for the experimenter or any object within range. His muscles are tense and crying is a common accompaniment. Such emotional display, together with the vigorous effort to right himself, reflects advanced development in ability to sense the situation. This phase is illustrated by *C* of figure 1. When no particular postural position was dominant, the records were scored by plus ratings in more than one phase.

D. Relaxed or Mature Phase.—The identifying feature of the fourth phase is the absence of marked flexion or extension. The child shows not only an awareness of the situation but an appraisal of the position with respect to his own neuromuscular potentialities. Even if he finds the inversion distasteful, he apparently realizes that strenuous effort to right himself is futile. The head hangs down in essentially the same plane as the shoulder and pelvic girdles, and the arms hang down toward the floor. Crying is uncommon when this phase has attained its maximum development. *D* of figure 1 represents the posture of the mature phase. In making ratings of this phase it was necessary to rely to some extent on certain qualitative aspects of the behavior rather than on the description of posture itself. The presence of transitional postures means merely that the development of flexor and extensor muscles is about equally strong, so that dominance of one or the other is not clearly indicated. Phase D, on the other hand, reflects not merely the equivalence of opposing forces but the integration of several sensory motor mechanisms which are necessary to the child's appraisal of the situation. Accurate rating of the older children was further complicated by the tendency of some to engage in a variety of activities which involve flexion or extension of the trunk merely as playful enterprises. When such instances occurred unmistakably as an act of play, a plus rating was made in phase D only, despite the manifestation of flexion or extension.

ANALYSIS OF DATA

After plus and minus ratings of the observational data had been made in accordance with the foregoing criteria, it was possible to plot the percentage of occurrence of each phase against chronologic age. The distribution of each phase is shown in the curves of figure 2. The data for phases A and B were averaged over twenty day intervals. Because of the longer age range, the data for phases C and D were

Occurrence of Phases A and B and C and D at Each Age Interval

Phases A and B		Phases C and D	
Age Interval in Days	Number of Observations	Age Interval in Days	Number of Observations
1- 20	134	1- 100	517
21- 40	102	101- 200	396
41- 60	99	201- 300	321
61- 80	93	301- 400	275
81-100	89	401- 500	239
101-120	86	501- 600	205
121-140	88	601- 700	225
141-160	74	701- 800	159
161-180	72	801- 900	93
181-200	76	901-1,000	90
201-220	60	1,001-1,100	58
221-240	73	1,101-1,200	53
241-260	60	1,201-1,300	47
261-280	74	1,301-1,400	35
281-300	54	1,401-1,500	24
301-320	59	1,501-1,600	23
321-340	58	1,601-1,700	21
341-360	59	1,701-1,800	19
361-380	48	1,801-1,900	11
381-400	51	1,901-2,000	8
401-420	56		
421-440	46		
441-460	58		
461-480	42		
481-500	37		
501-520	40		
521-540	38		
541-560	41		
561-580	36		
581-600	50		
601-620	35		
621-640	42		
641-660	49		

averaged over hundred day intervals. The number of observations at each age interval is indicated in the accompanying table.

It can be seen from the percentage curves of figure 2 that the flexor phase begins to decline about the end of the first month, that it drops rapidly during the next three months and is extinct in all children by the end of the fifth month. The extensor phase appears around the end of the first month; it is present in practically all babies between the ages of 4 and 6 months, begins to decline about the age of 6½ months and after the first year is almost invariably absent. Between the ages of 8 and 18 months the righting posture of phase C pre-

dominates. In some infants phase D appeared before the end of the first year, but for most of the children it was not characteristic until the second half of the third year.

The variability in the onset of phases C and D is much greater than in that of phase B. By selecting a twenty-five day interval and computing the percentage of infants in whom the emergence of any phase was manifested during each interval, the age range during which phases B, C and D were first manifested by different members of the group is shown. These distributions are illustrated by the curves in figure 3. The ogives show the total percentage of children in whom a particular phase was manifested at any given age. The curves of figure 4 show the percentage of infants who had completed a particular phase at any age period. At the age of 4½ months all the babies had completed phase A. Most of them had completed phase B before they

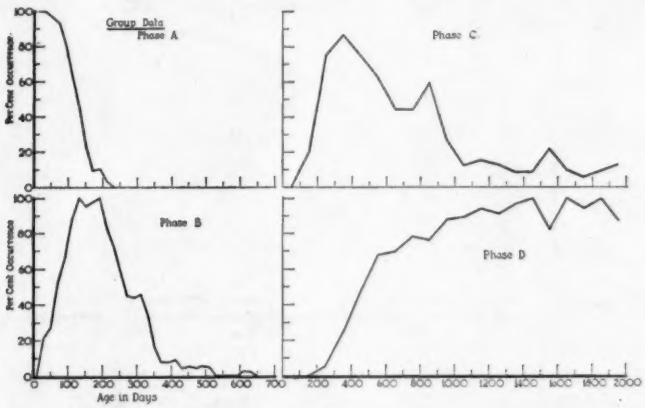

Fig. 2.—Curves showing on a chronologic scale the percentage distribution of each phase as manifested by the group.

were 9 months old, but completion has been recorded as late as at 14 months of age. The age at which phase C was completed varies from 11 months to 2 years, though in the majority of the children it was finished by the age of 18 months. Because of the paucity of observations, the data obviously are not so reliable for the higher age levels as for the earlier months. Nevertheless, the greater tendency toward variability in phases C and D in contrast to phases A and B is clearly evident. A factor which may contribute to the greater variability in the two later phases is that postural adjustment at this stage is more definitely influenced by the attitude or emotional status of the child at the moment of observation.

The common association of crying with phases A and C is indicated by the following percentages of occurrence: phase A, 86.5 per cent; phase B, 31.5 per cent; phase C, 83.9 per cent, and phase D, 10.0

per cent. This association of crying with a particular postural adjustment was often impressive during transitional phases, when the baby exhibited one or more postures during an observational period. For example, if for a moment the pelvis was flexed to right himself but as

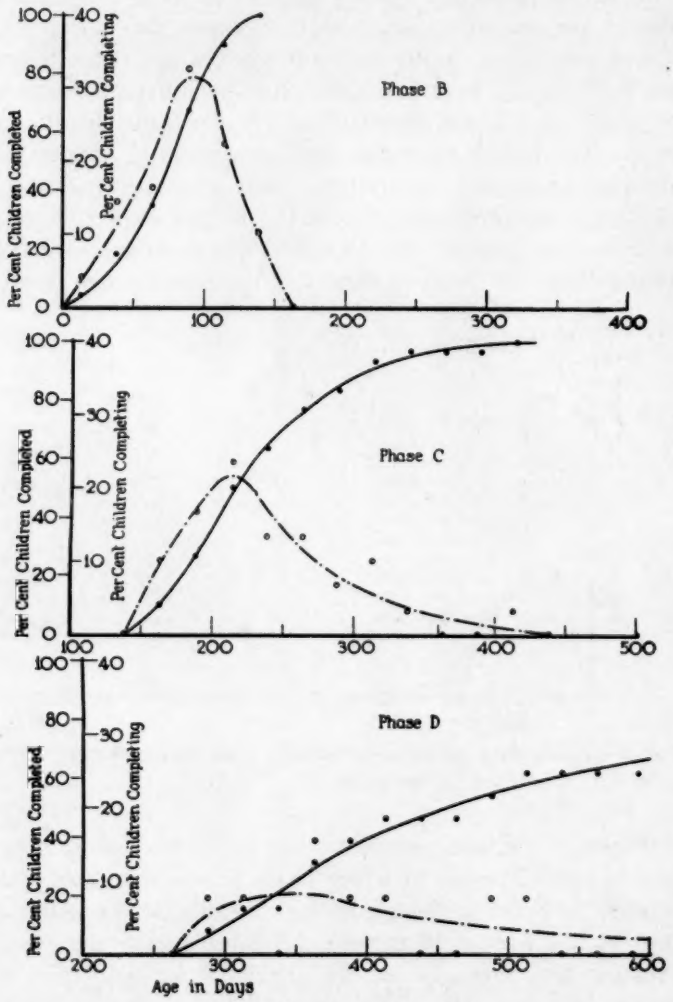

Fig. 3.—The curves in dotted lines indicate the percentage of infants at each age interval who showed the emergence of a phase at that time. The ogives show the total percentage of infants in whom the phase was manifested at any given age.

suspension time was lengthened the posture changed to spinal extension, it was frequently observed that crying accompanied the righting posture but that as soon as spinal extension appeared the crying stopped.

The longitudinal studies of the 4 children, in general, substantiate the results for the larger group. Two of these children were identical twin boys. The percentage of occurrence of each phase for these boys is shown in the curves of figure 5. Observations on these babies were

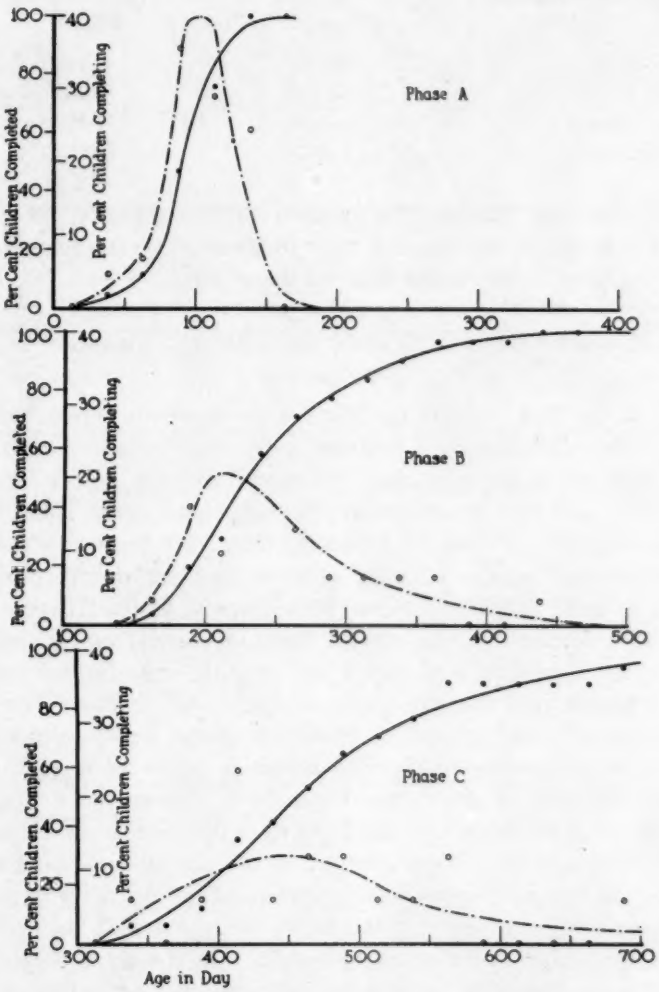

Fig. 4.—Dotted line curves show the percentage of infants in whom the phase was completed during each age interval. The ogives indicate the total percentage of infants who had completed a phase at any age level.

not begun until they were 100 days old; therefore, the percentages for the early occurrences of phases A and B were not obtained. Similarity in the curves for the twins is striking.

The percentage of occurrence of each phase in 2 unrelated girls is shown in figure 6. Interesting individual differences in the curves of

these 2 babies will be discussed later. These infants are still under observation, and since Patricia Shelley was slightly less than a year old at the time of this reporting, her curves for phases C and D are not complete. The incidence of crying associated with each phase for these 4 children is as follows:

	Phase A	Phase B	Phase C	Phase D
Jane Woods	98.1%	0	44.4%	0
Patricia Shelley	74.1%	0	3.3%	0
Charles Dalton	——	5.3%	71.0%	0
Peter Dalton	——	0	37.5%	3.6%

Despite the fact that daily repetition of the situation modifies the child's attitude, it can be seen that, in general, the individual records show the same trends as the data for the group.

DEVELOPMENTAL SIGNIFICANCE OF POSTURAL CHANGES DURING INVERSION

As in the case of other behavior of the newborn period, interpretation of the significance of postural adjustment to inversion can proceed from the assumption that the cerebral cortex is not functioning at birth. Anatomic investigations by both Conel [1] and Tilney [2] justify the assumption. It may be assumed, then, that the flexor posture of the suspended newborn infant is controlled by infracortical nuclei. Other studies [3] of neuromuscular development in this laboratory have supplied evidence that the earliest signs of cortical functioning are in the nature of inhibition of subcortical activity. In inverted suspension it is probable that the emergence of the spinal extensor phase is an expression of selective cortical inhibition of the flexion which characterizes the neonatal posture. Such inhibition paves the way for exercise and development of the extensor muscles. The universal presence in children of the extensor phase, together with its relative constancy at a particular age level, lends support to the assumption that the inception of the extensor response is predominantly subcortical in origin. Slowly the signs of cortical inhibition are supplanted by evidence of cortical activation of muscular movement. In the third phase, cortical control over muscular activity is indicated by the baby's deliberate effort to right himself. Not only has he gained cortical control over

1. Conel, J. L.: The Postnatal Development of the Human Cerebral Cortex, Cambridge, Mass., Harvard University Press, 1939.

2. Tilney, F.: The Structure and Development of the Brain, read at a staff conference of the Normal Child Development Study of the Department of Pediatrics, College of Physicians and Surgeons, Columbia University, New York, May 21, 1937.

3. McGraw, M. B.: Development of Neuro-Muscular Mechanisms as Reflected in the Crawling and Creeping Behavior of the Human Infant, J. Genetic Psychol., to be published.

muscular movement but also interconnections between various centers of the brain have matured; such connections contribute to the child's awareness of the situation. The straight, relaxed posture of the older child is an expression of the integration of several sensory and motor

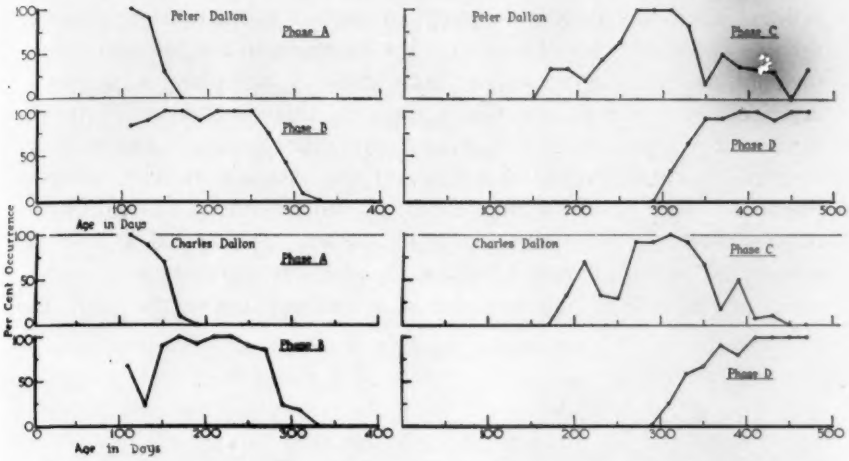

Fig. 5.—The age distribution of each phase of postural adjustment to inversion as manifested by identical twin boys.

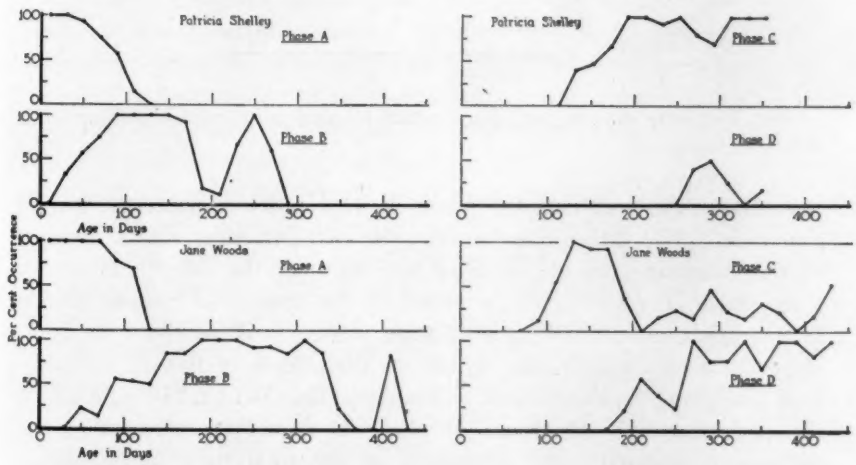

Fig. 6.—The age distribution of each phase of postural adjustment to inversion as manifested by 2 unrelated girls.

centers. The child's appraisal of the situation is complete; he has enough cortical control over flexor and extensor muscles to engage in any postural adjustment of his choice. Because of the integration of all these powers, he usually elects to do nothing but quietly acquiesce to the position imposed on him.

In an earlier discussion [4] of the process of behavior development, it was pointed out that organic behavior tends to oscillate between extremes before it settles down to an integrated system of action. The postural adjustment of the infant to inversion is peculiarly illustrative of this principle. The principle can be portrayed in a relatively simple fashion when the analysis is made in such a manner as to elucidate the two opposing types of activity. For example, in the postural adjustment of the infant to inversion, both phase A and phase C are characterized by action of the flexor muscles, though they differ in the degree of cortical control exercised over the flexion. Phase B, in contrast, is characterized by activity of the extensor muscles, whereas phase D is identified to a large extent by the absence of marked flexion or extension. It is possible, therefore, in any age interval to take the percentage of occurrence of phase A plus the percentage of occurrence of phase C as representative of a tendency toward flexion. The

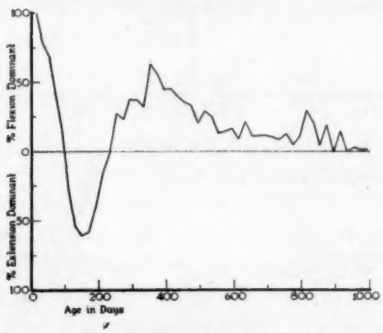

Fig. 7.—Curve showing the ages at which postural adjustment is predominantly flexion or extension.

percentage of occurrence of phase B represents a tendency toward extension. The differences between the two percentages is a measure of the dominance of one type of activity over the other. However, since phase D, which is characterized by the absence of marked flexion or extension, often overlaps with other phases, it is necessary to determine the actual time during which the dominance of flexion or extension could have been indicated. This actual time is found by subtracting the percentage of occurrence of phase D from 100 per cent. The remainder represents the percentage of the total time during which dominance could have been present. Relative dominance was therefore ascertained as a percentage of the previously determined difference between the percentages of occurrence of flexion and extension. That the dominance of flexion or extension is a function of chronologic age is clearly evident in the curve of figure 7. This curve not only illus-

4. McGraw, M. B.: Growth: A Study of Johnny and Jimmy, New York, D. Appleton-Century Company, Inc., 1935.

trates the dominance of flexion or extension as a function of age but shows that after the age of 8 months, when cortical flexion has become dominant, the trend is more fluctuating. In other studies [3] of neuromuscular development, greater variability has been observed during the more mature stages than during the early ones. Obviously, when more neural centers are operating in the performance of an activity, the possibility of variability increases.

In postural adjustment to inversion not only are the motor centers which govern somatic movements and position active but also, especially during the last two phases, the centers which control the conative or attitudinal aspects of behavior. The increasing influence of the centers which control conative aspects of behavior is expressed by changes in motor as well as in emotional behavior. This circumstance is well delineated in the adjustments of the children who were exposed to this situation frequently. These children manifested the mature or relaxed posture (phase D) at a much younger age than did the children who were tested only infrequently. However, with these children phase D was not sustained unless familiarity of experience was maintained. In the case of the twins, for example, phase D was established fairly well by the age of 400 days. Daily observations were terminated when they were 470 days old. They were returned to the laboratory for subsequent observations at biweekly or monthly intervals. Despite the fact that phase D had become dominant, both children during the period of infrequent observations regressed to the flexed posture characteristic of phase C. Indeed, intensive study of individual children has suggested the possibility of using the child's adjustment to inversion as an indicator of individual balance between conative and somatic factors in the general behavior.

There appear to be definite individual differences in the extent to which an altered attitude may interrupt the pattern of somatic development. This point may be clarified by the contrasting behavior of Patricia Shelley and Jane Woods. Considerable neuromuscular tension and crying is, in most children, a concomitant of phase C. Patricia Shelley, as a result of daily exposure to the situation, early developed an acquiescent attitude. She did not cry nor was she particularly tense. However, this acquiescent attitude had little effect on the motor aspect of her adjustment. Day after day she continued to flex in the righting posture although she showed no sign of emotional disturbance. It appeared as if the organization of motor mechanisms was dominant and proceeded with regularity, despite the alteration in attitude. Other children, notably Jane Woods, showed a dominance of conative functioning. The motor pattern was determined to a large extent by the emotional status at the time of observation. The somatic pattern, after the onset of phase B, was less clear and less well sustained. While all phases were manifested, there was considerable over-

lapping of phases B, C and D. Despite the inconsistency of motor pattern, this child showed a greater frequency of tension and crying during phase C than did Patricia Shelley. From general observation of the 2 children in other activities, these differences appear to reflect individual peculiarities which permeate their behavior.

Other examples could be offered, but these suffice to illustrate the point that development of organic neuromuscular functioning is more extensively influenced in some children than in others by the maturation and exercise of attitudinal factors and that these differences represent individual traits.

SUMMARY

Postural adjustments of the infant when held in a position of suspended inversion have been classified into four distinct phases. The classification of these phases was based on 2,841 observations of 77 children over a period of five years plus longitudinal (daily) observations on 4 additional infants during the first twelve or eighteen months of life.

The phases as described occur in serial order and are of developmental import. They appear to reflect maturational changes in the central nervous system.

The newborn phase, characterized by flexion, is probably controlled at a subcortical level. This period of nuclear flexion extends over the first four months but is most evident during the first thirty days of life.

It is followed by a period of hyperextension of the vertebral column. The quality of the extensor response and its relative constancy suggest that the extensor phase also is of subcortical origin, though its inception is probably facilitated by selective inhibitory influences from the cortex. The extensor response is most common between the fourth and the sixth month of age, though it may be elicited later.

The righting phase, which is characterized by marked pelvic flexion in a deliberate attempt to regain the upright posture, reflects cortical dominance of the neuromuscular movements involved; the accompanying emotional status of the child reflects the involvement of sensory mechanisms which influence the somatic adjustment.

The relaxed or mature phase reflects not only the involvement but the integration of several sensory and motor centers which function in the child's appraisal of the situation. Such advanced comprehension tends to evoke a relaxed or playful postural adjustment.

The functional level and the involvement of various neural centers are reflected by both the affective and the somatic aspect of the behavior pattern. Crying is commonly associated with the newborn (A) and the righting (C) posture and only infrequently occurs during the extensor (B) or the mature (D) phase.

CHORIONIC GONADOTROPIC EFFECTS ON GROWTH IN SEXUALLY UNDERDEVELOPED OLDER BOYS

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It has been found and reported by me,[1] as well as by others,[2] that too intensive treatment with chorionic gonadotropin, given for sexual underdevelopment, produces in some patients precocious secondary sexual characteristics. In view of this fact, it is important to know what specific effects intensive treatment, or for that matter what effects nonintensive administration of chorionic gonadotropin, has on height and osseous development as well as on sexual development.

In a recent paper[1a] on my observations on the skeletal changes produced in 9 young boys, between the ages of 3 years 3 months and 8 years, who were given varying doses of chorionic gonadotropin for sexual underdevelopment, I reported that height was increased and ossification was accelerated in most of the patients.

From the Endocrine Clinic of the Department of Pediatrics, New York University College of Medicine, and the Children's Medical Service of the Third Medical Division, Bellevue Hospital, Dr. Charles Hendee Smith, director.

1. Dorff, G. B.: (*a*) Chorionic Gonadotropic Effects on Height and Osseous Development in Sexually Underdeveloped Young Boys, Endocrinology **27**:403 (Sept.) 1940; (*b*) Maldevelopment and Maldescent of the Testes: I. Report of Treatment with the Anterior Pituitary-Like Gonadotropic Hormone from the Urine of Pregnant Women, Am. J. Dis. Child. **50**:649 (Sept.) 1935; (*c*) II. Further Observations on Treatment with Anterior Pituitary-Like Gonadotropic Hormone, ibid. **50**:1429 (Dec.) 1935; (*d*) III. Treatment of the Several Types of Adiposogenital Dystrophy in Boys, with Particular Reference to the Use of Gonadotropic Hormone from the Urine of Pregnant Women for Their Imperfectly Developed Genitals, J. Pediat. **8**:704 (June) 1936; (*e*) IV. The Treatment with Gonadotropic Hormone (Anterior Pituitary-Like) of Nonadipose Boys Showing Genital Dystrophy, ibid. **10**:517 (April) 1937; (*f*) Intra-Abdominal Cryptorchidism Treated with Gonadotropic Substance: V. Observations in a Series of Twelve Prepuberal Boys, J. A. M. A. **110**:1799 (May 28) 1938.

2. Thompson, W. O., and Heckel, N. J.: Precocious Sexual Development from an Anterior Pituitary-Like Principle, J. A. M. A. **110**:1813 (May 28) 1938. Thompson, W. O.; Heckel, N. J.; Thompson, P. K., and Dickie, L. F. N.: Further Observations on the Treatment of Hypogenitalism and Undescended Testes, with Special Reference to the Production of Premature Puberty, Endocrinology **22**:59 (Jan.) 1938. Turner, H. H.: Anterior Pituitary Gonadotropic and Anterior Pituitary-Like Hormone in the Treatment of Cryptorchidism, South. M. J. **31**:381 (April) 1938.

I also reported that 8 of the boys in this series (the exception is the youngest, who is now only 6 years old) have reached an age between 10 and 14 without signs of any further acceleration in growth; they seem to be continuing along the curves established as a result of treatment. I found no evidence of premature union of the epiphyses in these patients.

While such results were gratifying, I felt it wise, because of some other observations made in this study, to revise my former stand and to suggest that generally treatment should not be started at too early an age. The results of therapy in the youngest boy in my series, who is now only 6 and whose treatment for the correction of intra-abdominal testes was instituted at the early age of 3 years 3 months, will serve as an example. Only a partially successful result had been produced when it became obvious that treatment would have to be discontinued because of further enlargement of an originally enlarged phallus and too rapid advance in height and ossification. The boy attained a height curve on Burgess' growth chart of over 99 per cent, while the original curve had been 75 per cent; he showed an osseous age from 2 to 2½ years in advance of his chronologic age, while originally his osseous age had been advanced only by 1 or 1½ years.

Keeping in mind, therefore, the possibility of such occurrences in other patients, I suggested that for general use, with a few exceptions, treatment with chorionic gonadotropin for cryptorchidism and hypogenitalism should not be instituted before the age of 5 years and should be given cautiously and judiciously at all times.

I made this suggestion because I feel that sufficient time has not elapsed since the termination of treatment of these young boys to foretell what developments may take place in the far future. I did not, however, feel then, nor do I feel now, that there is any possibility that developments are imminent which would lead to a condition similar to macrogenitosomia. This condition was not found in any of my patients, even after a relatively long follow-up period and even though some of the external manifestations seemed to be similar.

In this paper I am reporting on a study of older boys similar to that made of the younger boys, that is, a study of the effects on height and ossification of administration of chorionic gonadotropin to boys between the ages of 8 and 15 years.

For convenience in discussion, I divided the patients into three groups according to the age at which they received treatment: (1) between the ages of 8 and 10 years, (2) between the ages of 10 and 13 and (3) between the ages of 13 and 15.

It is not the purpose of this report to detail the gonadal or genital responses provoked by chorionic gonadotropin,[3] for these have already been reported in detail in previous communications. I simply wish to state that all the patients included in this series showed definite sexual changes as a result of treatment; in some the genital development was complete and in others only partial.

I used the growth charts of Burgess,[4] which I found helpful. I also used in this study the standards for ossification given by Flory[5] and by Todd.[6]

OBSERVATIONS ON PATIENTS

This report is based on 21 patients with genital dystrophy, 20 of whom for the most part received continuous and intensive treatment with chorionic gonadotropin for sexual underdevelopment and some of whom received, in addition, small amounts of desiccated thyroid. One patient received only desiccated thyroid. He was included in this series for comparison because some interesting results were achieved.

Genital dystrophy exists both in the adipose boy and in the non-adipose, the former occurrence being the more prevalent. It may exist in tall, normal or stunted boys, usually being more common in tall boys. It may exist, too, in those showing normal, advanced or even retarded osseous development.

Included in this series were only those patients who could be followed up for a reasonably long time after the termination of treatment.

The youngest boy was 8 years 2 months of age when treatment was started; the others ranged from 8 to 15 years of age. Some of these patients have been under observation for as long as 8 years, with a follow-up period in some instances of from four to six years after termination of treatment.

In almost all of the patients under 13 years of age, treatment with chorionic gonadotropin in due time caused, even though temporarily in some instances, some acceleration of the growth in height. With the exception of patient 30, this effect was particularly evident in the moderately tall and in the relatively stunted boys who received initial treatment before the age of 13 years.

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3. The chorionic gonadotropin used in these studies was supplied in part by E. R. Squibb and Sons (follutein), Ayerst, McKenna and Harrison (A. P. L.), Parke, Davis and Company (antuitrin S), by the Winthrop Chemical Co. (korotrin), by the Schering Corporation (pranturon) and by Roche-Organon, Inc. (pregnyl).

4. Burgess, M. A.: The Construction of Two Height Charts, J. Am. Statist. A. **32**:290 (June) 1937.

5. Flory, C. D.: Osseous Development in the Hand as an Index of Skeletal Development, Monographs of the Society for Research in Child Development, National Research Council, 1936, vol. 1, no. 3.

6. Todd, T. W.: Atlas of Skeletal Maturation, St. Louis, C. V. Mosby Company, 1937.

TABLE 1.—*Observations on Twenty Boys Treated with Chorionic Gonadotropin and One Boy Treated with Desiccated Thyroid Alone for Sexual Underdevelopment*

	Before Therapy with Gonadotropin				Total Dosage in Rat Units; Duration of Treatment	After Therapy with Gonadotropin				At End of Study				
Patient	Percentile Height Curve (Burgess) %	Chronologic Age in Years and Months	Osseous Age in Years and Months: Flory	Osseous Age in Years and Months: Todd		Percentile Height Curve (Burgess) %	Chronologic Age in Years and Months	Osseous Age in Years and Months: Flory	Osseous Age in Years and Months: Todd	Percentile Height Curve (Burgess) %	Chronologic Age in Years and Months	Osseous Age in Years and Months: Flory	Osseous Age in Years and Months: Todd	Comment
10	40 40	7:8 8:9	6:0 8:0	6:0-3 7:3-9	..... 46,635 11 mo.	.. 60 72	.... 9:9 10:9	.... 12:0	.... 11:9-12	.. 66	.... 14:1	.... 17:0	.... 16-6:9	Desiccated thyroid administered for 9 mo. 1 year prior to administration of gonadotropin; lag in osseous age diminished by about 6 mo.; highest height curve 82%
11	36	9:9	8:0	7:3-6	57,000 9 mo.	53	10:7	....	....	52	12:7	12:6-12	12:3-6	Desiccated thyroid administered with chorionic gonadotropin
12	88	9:3	10:0-6	9:3	36,600 15 mo.	96	11:5	....	....	95	14:0	15:6	15:9-12	Desiccated thyroid administered at irregular intervals with chorionic gonadotropin
13	58	8:8	9:6	8:9	39,250 10 mo.	78	9:5	10:0	11:3-6	64	13:11	14:6	14:3	Desiccated thyroid administered for short periods before and after administration of chorionic gonadotropin
29	60 86 97	6:0 8:11 10:11	6:0	5:9	..... 57,900 12 mo. 3,400 2 mo.	.. 90 99	.... 10:1 11:1	.... 13:0	.... 13:9	..	....	....	....	Desiccated thyroid administered for 2 mo. prior to administration of chorionic gonadotropin; rising height curve from 60 to 80% between 4:11 and 8:11; discontinued first period of treatment because of illness; still under treatment with chorionic gonadotropin
30	.. 38	7:6 8:1	5:0 ...	5:9 ...	..... 101,300 17 mo.	.. 30	.... 9:6	.... 8:0-6	.... 7:3	.. 22	.... 11:6	.... 10:0	.... 9:9-10:3	Some desiccated thyroid administered prior to chorionic gonadotropin; administration of desiccated thyroid for a short time with chorionic gonadotropin; depressed height curve
14	93 94	7:5 9:11	... 10:6	... 11:3	..... 63,550 15 mo.	.. 98	.... 11:7	.... 14:0	.... 13:9	.. 78	.... 15:5	.... 16:0	.... 16:6	Desiccated thyroid administered for 18 mo. prior to administration of chorionic gonadotropin
15	99+ (1 in 5,000)	10:6	12:6-12	12:6-9	265,150 24 mo.	99+ (1 in 4,000)	12:6	....	....	99+ (1 in 5,000	13:8	15:0	14:9	Desiccated thyroid administered for 18 mo. during treatment with chorionic gonadotropin

16	40	11:5	9:0	8:9	82,610 15 mo.	50	13:3	12:0	11:3	75	15:3	14:6	14:3	Desiccated thyroid not administered
17	14 19	10:5 11:0	.... 10:0	.... 10:3	..... 96,900 18 mo.	.. 40	.... 12:6	....	....	.. 65	.... 12:10	.... 12:6	.... 13:3	Desiccated thyroid administered throughout period of treatment; none thereafter
18	93	10:7	11:0	10:3-9	46,266 13 mo.	97	11:7	12:6	12:0-3	86	15:10	17:6-12	16:9	Desiccated thyroid not administered
19	97	11:9	13:0	13:3	11,900 9 mo.	96	12:6	....	....	85	15:8	17:0	16:9	Desiccated thyroid administered 9 mo. after administration of chorionic gonadotropin at irregular intervals; irradiation of thymus in infancy
20	70	10:9	9:0-6	10:6-9	33,400 24 mo.	84	12:8	....	....	79	15:7	17:0	16:9	Desiccated thyroid administered throughout treatment with chorionic gonadotropin
21	99+ 99+	10:1 11:0	13:0	12:9	..... 59,000 24 mo. (irregular)	.. 99 98	.... 13:1 13:10	.... 15:6	.... 15:9	.. 93	.... 14:10	.... 17:6	.... 17:0	Desiccated thyroid not administered
23	50	10:4	10:0	9:9	26,000 4 mo.; 17,000 1 mo. (1 yr. later)	61	10:7	....	....	64	14:4	16:0	16:0-3	Two periods of gonadotropic therapy; desiccated thyroid given for 1 month during treatment with chronic gonadotropin
22	2+	15:10	12:0	12:9	No chorionic gonadotropin	..	....	....	....	32	20:3	17:6-12	17:3	Little growth in height for 5 yr. prior to age 15:10; no medication prior to that age; desiccated thyroid given since then to date
24	42	14:4	14:0	14:3-6	18,625 9 mo.	45	15:1	....	....	50	18:4	17:0	16:9	Desiccated thyroid administered with chorionic gonadotropin; desiccated thyroid given at irregular intervals subsequently
25	60	13:9	13:6	13:0-3	41,750 10 mo.	55	14:6	....	....	63	15:9	15:0-6	15:6-9	Desiccated thyroid administered with chorionic gonadotropin; none thereafter
26	18	14:6	13:0	13:3	42,100 8 mo.	22	15:4	....	....	24	15:8	14:0	15:3	Desiccated thyroid administered with chorionic gonadotropin
27	80	13:2	12:6-12	12:6-9	208,100 22 mo.	80	15:0	....	....	86	16:1	15:0	15:3-6	Desiccated thyroid administered with chorionic gonadotropin
28	32	13:2	14:0	13:9-14:3	25,000 6 mo.	32	13:7	....	....	19	17:2	18:0	18:0-3	Desiccated thyroid administered with chorionic gonadotropin; irradiation of thymus in infancy

* My own interpretations of osseous development based on Shelton's standards are not as advanced as those of Todd or of Flory. They fall short of the latter standards by from six to eighteen months, particularly in those patients under 13 years of age.

Patient 30, a stunted boy, was the only one in the group of moderately tall or relatively stunted boys who showed a depressed rather than an accelerated rate of increase in height during and after treatment. I believe that he did not respond because his condition was primarily one of marked thyroid insufficiency, with only secondary involvement of the genitals. This situation was made evident by the fact that his genital response to chorionic gonadotropin was good, yet he showed no corresponding advance in height similar to that made by my other patients. This patient was given dessicated thyroid without showing any favorable response in height, although his osseous advance was fairly well maintained for the period of study. It is possible that he needed continuous treatment with larger doses of desiccated thyroid.

Increase in height was not as evident for the very tall boys as it was for the moderately tall or stunted boys. However, it was evident, even though slight, in all but 2 of the very tall boys. In the 2 boys who showed no acceleration of growth in height (patients 15 and 21), there was no apparent change in the height during the period of treatment.

In all the boys ranging in age between 13 and 15 at the time treatment was instituted, with 1 exception, patient 26, there was no appreciable acceleration of the growth in height regardless of the original height. Patient 26, the 1 exception, showed a slight increase in height during treatment.

Judging from my patients, I should say that the younger the boy is the better are his chances for stimulation of growth in height through gonadotropic therapy and that as a rule the stunted and the moderately tall boys are more likely to show a more pronounced and significant acceleration of growth in height than the very tall boys.

One notes that in some of the patients in this series whose treatment was started not early but rather later, at the age of 10 years or more (patients 10, 12, 14, 18, 19, 21 and 28), a lapse of time has shown some tendency toward tapering off of the height curves. It is possible, therefore, that they are beginning to terminate their growth a year or so before the time indicated as normal by Burgess' growth chart. This, of course, does not necessarily mean that the height each boy was destined to attain has not been reached. Possibly the ultimate height simply was attained sooner than if the boys had grown at a slower pace. This suggestion is mere conjecture, since one would have to know the trend of these height curves for many years before the institution of therapy to determine its validity. However, such an assumption would fit in with the expectation, indicated on Burgess' chart, that rapidly growing boys terminate growth sooner than those who grow slowly.

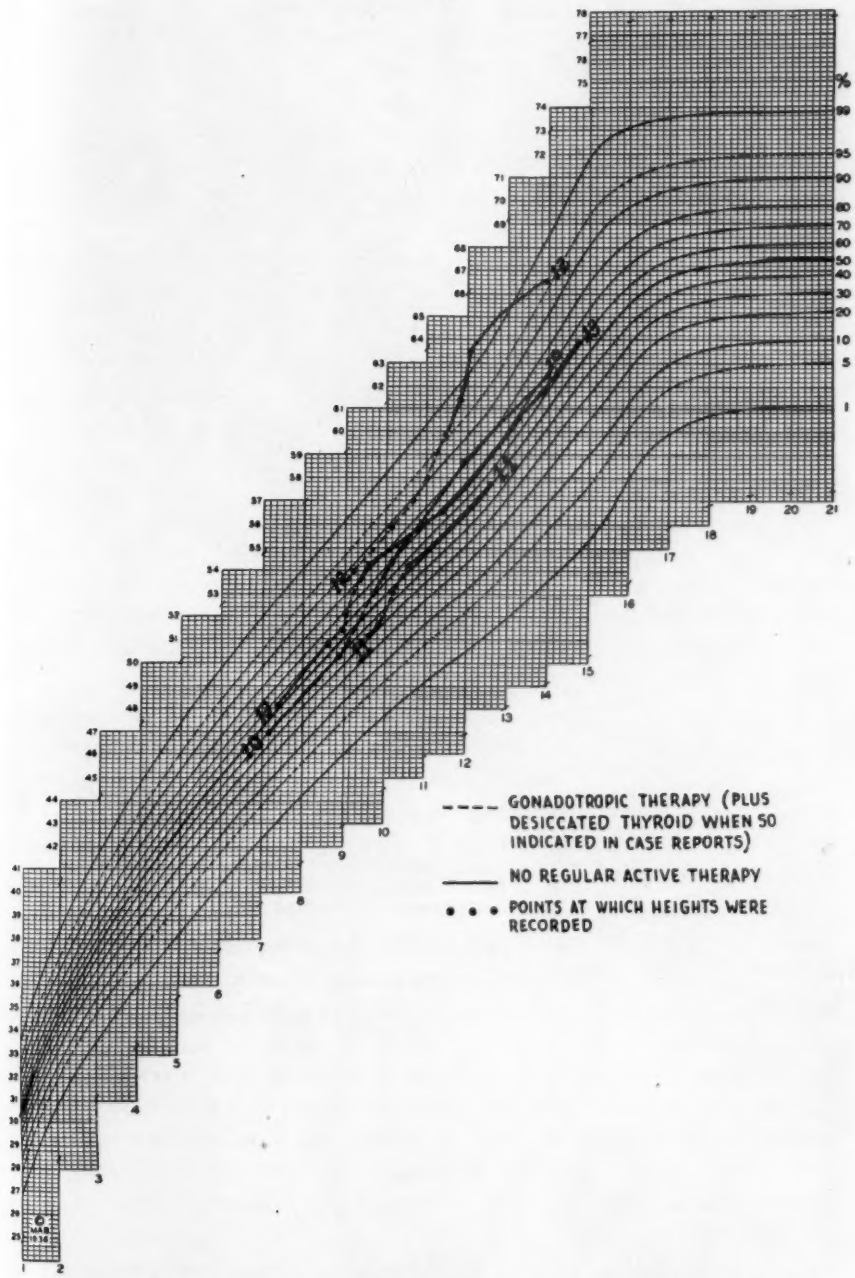

GONADOTROPIC THERAPY (PLUS DESICCATED THYROID WHEN SO INDICATED IN CASE REPORTS)
NO REGULAR ACTIVE THERAPY
POINTS AT WHICH HEIGHTS WERE RECORDED

Chart 1.—Height curves for 4 boys whose treatment with chorionic gonadotropin was begun between the ages of 8 and 10.

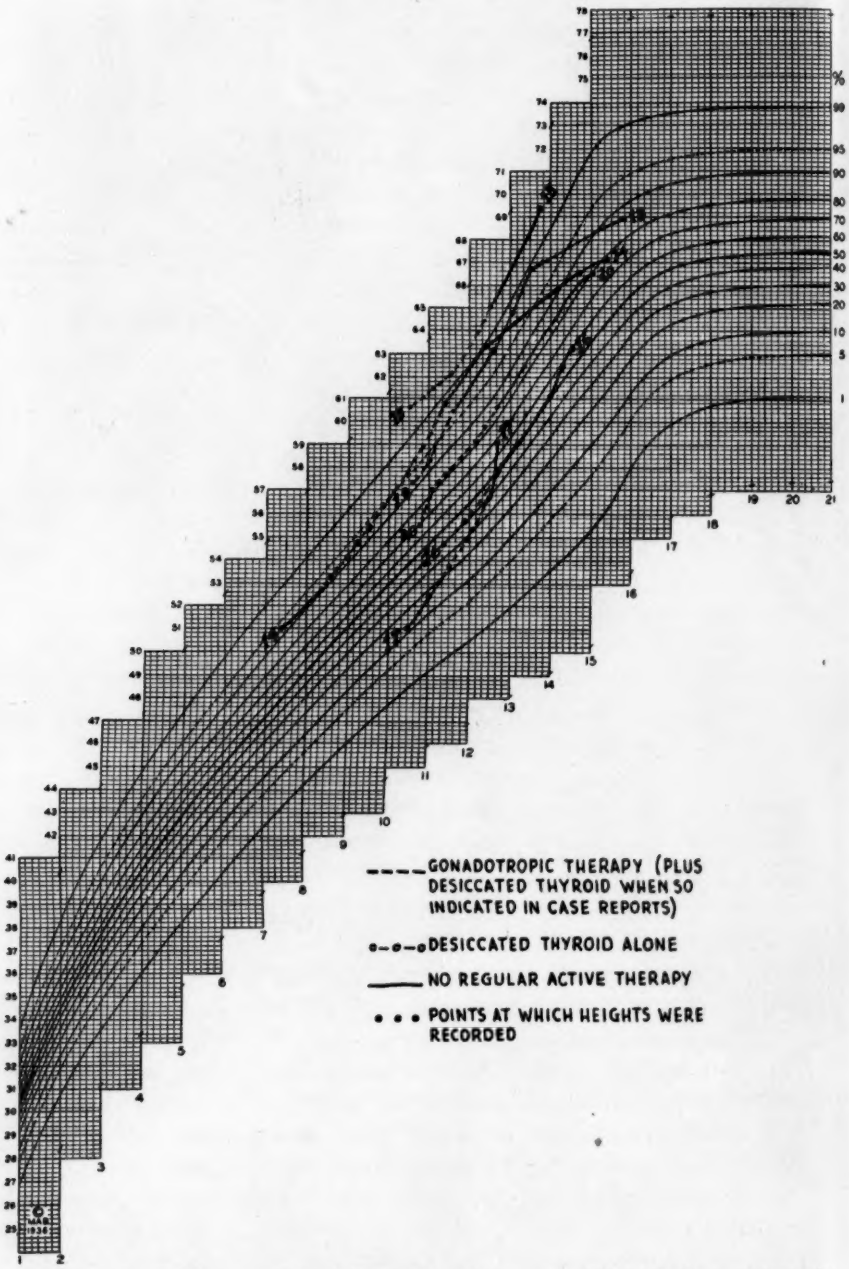

GONADOTROPIC THERAPY (PLUS DESICCATED THYROID WHEN SO INDICATED IN CASE REPORTS)
DESICCATED THYROID ALONE
NO REGULAR ACTIVE THERAPY
POINTS AT WHICH HEIGHTS WERE RECORDED

Chart 2.—Height curves for 6 boys whose treatment with chorionic gonadotropin was begun between the ages of 10 and 13.

With regard to patients 18 and 21, mentioned previously, there is a suggestion that the final percentile height curve will even be below the curve which existed at the outset of treatment. These patients do not present much cause for worry, since they are tall and a slightly lower final height will not matter much. A tapering off of height might even be a distinct advantage in the very tall boys who otherwise might have a tendency toward attaining too great a height.

It was noted in my first series of patients, whose treatment was started when they were very young, that an accelerated height curve attained by a patient seemed to maintain itself without any noticeable tapering off. It is true, however, that the observations on these patients are not conclusive, since they have not been followed up long enough for one to tell what the final outcome will be. There is the possibility, although it is only conjectural, that tapering off in height will also occur in the young boys whose treatment was started before the age of 10 years.

Ossification, as a rule, was stimulated in the greater number of patients in my series of older boys, just as it was in the boys under 8 years of my previous series. It appears that the younger the boy when such stimulation took place, the greater was his osseous advance.

In most of the patients under 10 years of age, the osseous increment during the period of treatment was greater than the increment normally expected for that chronologic period; there was a further advance in an already originally advanced osseous age, an advance in an originally normal osseous age or a diminution of an original lag in those patients who had a retarded osseous age.

In some of the patients between 10 and 13 years of age, osseous increments above those normally expected were also noted, but the increments were not as great as they were in the younger boys previously mentioned.

In the boys between 13 and 15 years of age, there was no clearcut evidence of any unusual acceleration of ossification; there was simply an apparently normal advance commensurate with the chronologic lapse of time.

Changes in ossification were noted in all types of patients, that is, in the tall, the moderately tall and the stunted.

There seemed to be no constant correlation between the acceleration of growth in height and the advance in ossification.

In the patients in whom growth in height is tapering off and ossification is being accelerated, as in patient 18 and perhaps in patient 28, one might expect early termination of growth by epiphysial closure. On the other hand, in those patients in whom increase in height is being maintained or is tapering off and progress in ossification is

retarded, as in patients 21, 24 and 27, theoretically one would assume that with the proper stimulus an increase in height could still be attained.

TABLE 2.—*Effect of Treatment with Chorionic Gonadotropin on Osseous Development*

Patient	Duration of Study in Yr. and Mo.	Increase in Osseous Development *		Osseous Development †		Summary
		Flory	Todd	Beginning of Therapy	End of Therapy	
10	6:5	11:0	10:6	—	+	Increased growth in height and osseous development
11	2:10	4:6-5:0	5:3-6:0	—	N—	Increased growth in height and osseous development
12	4:9	5:0-5:6	6:6-6:9	N+	+	Increased growth in height and osseous development
13	5:3	5:0	5:6	N+	+	Increased growth in height and osseous development
29	5:1	7:0	8:0	N—	+	Increased growth in height and osseous development
30	4:0	5:0	4:0-4:6	—	—	Decreased growth in height and increased osseous development
14	5:6	5:6	5:3	+	+	Growth in height increased and now tapering off; increase in osseous development maintained
15	3:2	2:0-2:6	2:0-2:3	+	+	Increased growth in height maintained; rate of osseous development decreased
16	3:10	5:6	5:6	—	—	Increased growth in height and osseous development
17	1:10	2:6	3:0	—	N+	Increased growth in height and osseous development
18	5:3	6:6-7:0	6:0-6:6	+	+	Growth in height increased and now tapering off; osseous development increased
19	3:11	4:0	3:6	+	+	Growth in height maintained and now tapering off; osseous development maintained
20	4:10	7:6-8:0	6:0-6:3	N—	+	Growth in height and osseous development increased
21	4:9	4:6	4:3	+	+	Growth in height maintained and now tapering off; rate of osseous development maintained or slightly decreased
23	4:0	6:0	6:3-6:6	—	+	Growth in height and osseous development increased
22	4:5	5:6-6:0	4:6	—	—	Growth in height and osseous development increased
24	2:8	3:0	2:3-2:6	N—	—	Growth in height increased; osseous development decreased
25	2:0	1:5-2:0	2:6-2:9	—	N—	Growth in height maintained; rate of osseous development maintained or slightly increased
26	1:2	1:0	2:0	—	—	Growth in height increased; rate of osseous development maintained or slightly increased
27	2:11	2:0-2:6	2:9	—	—	Growth in height increased; rate of osseous development maintained or slightly decreased
28	4:0	4:0	4:0-4:6	+	+	Growth in height maintained and now tapering off; rate of osseous development maintained or slightly increased

* The use of two standards at variance with each other gave rise to two readings.
† N stands for normal osseous development, the minus sign for retarded osseous development and the plus sign for advanced osseous development.

It is of interest to note that in 1 patient (no. 15) treated with the large total dose of 265,000 rat units over a period of two years, accelerated growth in height and advance in ossification did not occur, even though a good sexual response was obtained.

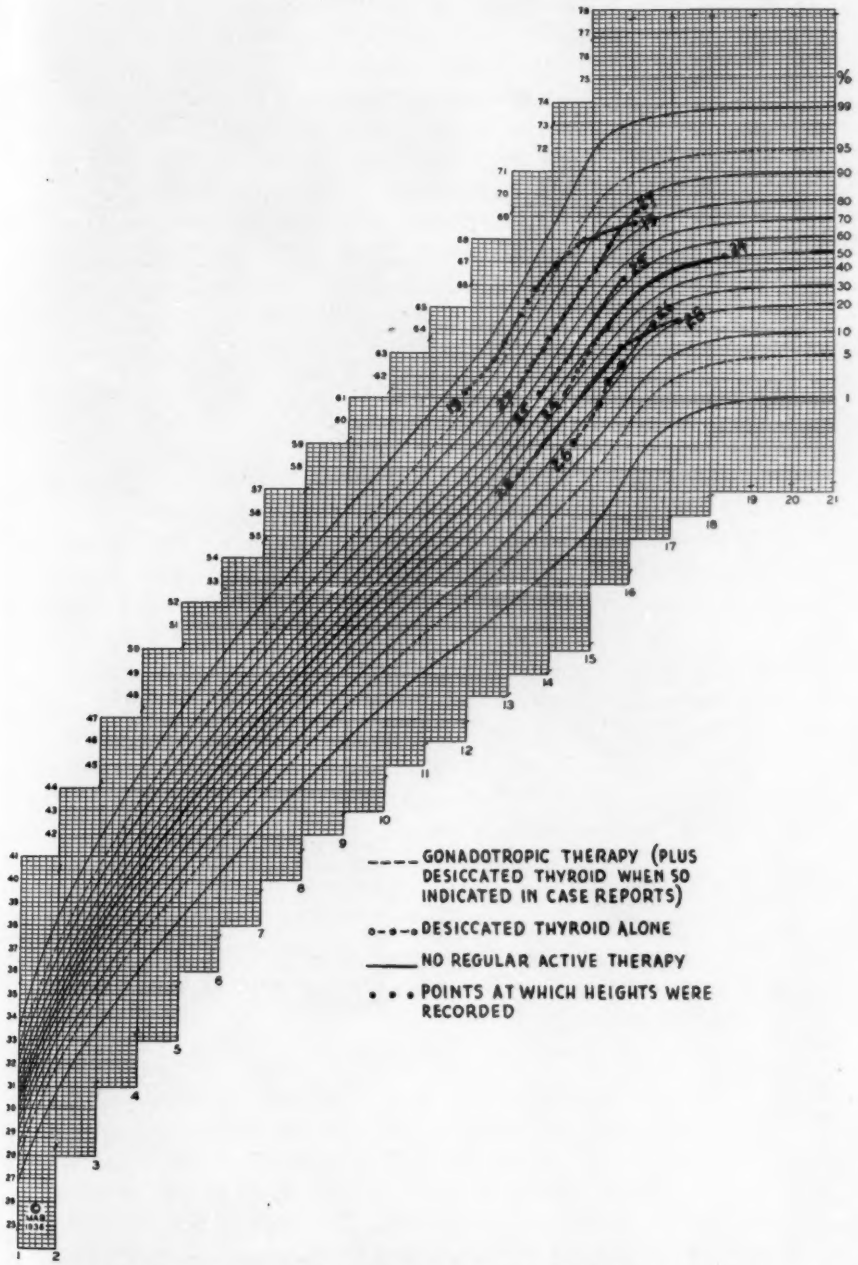
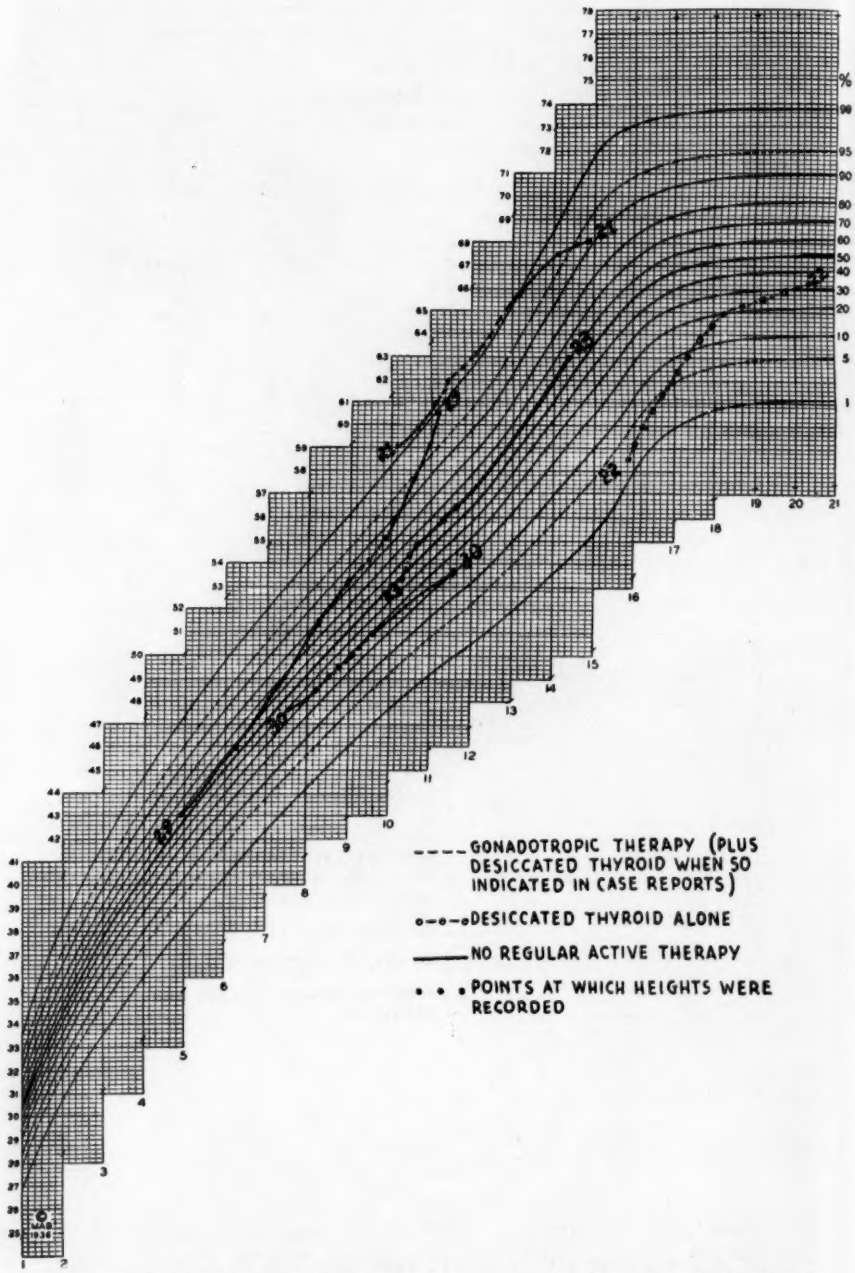


Chart 3.—Height curves for 6 boys whose treatment with chorionic gonadotropin was begun between the ages of 12 and 15.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%

Chart 4.—Height curves for 4 boys treated with chorionic gonadotropin and 1 boy treated with desiccated thyroid alone.

I am aware that in some of the patients in whom desiccated thyroid was used in addition to chorionic gonadotropin, the thyroid may also have played some part in accelerating growth in height and in advancing osseous development. Patient 22, included in this group to illustrate the effect of thyroid therapy on growth, is the most outstanding example. This patient when seen by me at the age of about 16 years was sluggish, markedly stunted in height and about three or three and a half years retarded in ossification. His genitals were hypoplastic. He had adiposogenital dystrophy, which seemed to me to be due primarily not to hypogonadism but to marked thyroid insufficiency. Desiccated thyroid rather than chorionic gonadotropin was administered therefore. After treatment with desiccated thyroid, it was noted that genital development was stimulated and that the patient's height curve had advanced from 2.5 per cent to 32 per cent over a period of about four and a half years. In addition his osseous development kept fairly good pace with his chronologic age. It is true, however, that at the time of this study, when the patient was 20 years 3 months of age, he still showed osseous retardation of about two and a half or three years. I do not believe though that at the late age of 16, when treatment was started, chorionic gonadotropin alone could have accomplished what desiccated thyroid accomplished alone or what chorionic gonadotropin has been found to accomplish in younger boys.

The extent to which height curves and progress in osseous development in my patients have been modified by gonadotropic therapy is an interesting speculation. Whether the final height of these boys was modified in any way or whether the end result was simply hastened, without affecting the ultimate height that would have been attained in any event, is not known. To answer such questions requires a much greater fund of information than is now available.

Too great concern about lasting ill effects from treatment with chorionic gonadotropin need not exist, I believe, since, as far as I have found in any of my patients, nothing too alarming has taken place or seems imminent. On the contrary, many good effects have been achieved.

SUMMARY AND CONCLUSION

This report is based on a study of the effects on growth in height and progress in ossification in boys between the ages of 8 and 15 years given chorionic gonadotropin for the correction of cryptorchidism, hypogenitalism or both. In this series were 20 boys who were treated in this way, and in addition 1 adolescent boy who had not only adiposogenital dystrophy but marked hypothyoidism, for which desiccated thyroid rather than chorionic gonadotropin was administered. This case was included for comparative purposes.

In spite of inadequate data on height curves before the institution of therapy and in spite of the insufficient length of time for following up some of these patients, although six years have elapsed since termination of the treatment of some, the effects on growth in height and progress in ossification of continuous, intensive treatment with chorionic gonadotropin for genital dystrophy can nevertheless be evaluated to some extent.

Increase in height took place in the moderately tall or stunted boys, particularly in those in whom treatment was started before the age of 13 years. No appreciable change in height took place in the greater majority of those whose treatment was started between the ages of 13 and 15. One stunted boy, however, who was 14½ years of age, responded by a slight rise in his height curve. As a rule, no appreciable increase in height occurred in the very tall boys in any age group. Generally speaking, it can be said that the younger the boy when treatment begins, the greater is his chance for increased height, particularly if he is stunted or only moderately tall.

It is not known conclusively at this time whether gonadotropic therapy has changed the final height to be attained by these patients or whether it has only hastened the rate of growth to some small degree, without actually affecting the normal end result that is to be attained.

Acceleration in osseous development occurred in most patients, as judged roentgenographically in the carpus by the appearance and contour of the centers of ossification and epiphysial nuclei. This acceleration was prominent in those boys under 13 years of age and less evident in those over 13, although undoubtedly many changes took place in them too. In general, either the osseous development which originally was normal was advanced by treatment beyond that normally expected or the osseous development which originally was advanced beyond the chronologic age was advanced still further. In other instances, an originally retarded state of osseous development was corrected, sometimes to the point of completely overcoming the lag or of even advancing the osseous age. In some patients this advance did not overcome the lag completely, in spite of progress and a lapse of several years after discontinuance of treatment. In some, on the other hand, simply the same normal or advanced rate of development was maintained.

There was no evidence of any gross abnormality in ossification following treatment in the older boys between 8 and 15 years, some of whom were followed up for six years after termination of treatment, just as there was no evidence in my previous series of younger boys under 8, some of whom were followed up for four years after termination of treatment. In neither the young boys of my other series nor in the older boys in this series was there evidence of any premature

closure of the epiphyses. There was noted, though, after a follow-up examination, some suggestion of an attempt at union earlier by about a year than that indicated as the average normal for the chronologic age by the standards set up by Flory and by Todd. Such earlier closure of the epiphyses in very tall boys as was accomplished in patient 21 might be of advantage if it could curtail excessive increments in height.

Generally speaking, the chance for acceleration and advance in ossification is greater in younger boys.

I do not subscribe to the belief, entertained by some, that the results from administration of chorionic gonadotropin can be compared to the uncontrollable and pathologic disorder of macrogenitosomia.

Dr. May Ayres Burgess, who originated the growth chart used in this report, and Dr. Josephine H. Kenyon aided me in the interpretation of the charts.

Misses Nell Cook, Ann Soscia, Virginia Harris, Angelina Lucier and Mrs. Marie L. Parker, of the nursing staff of the Children's Clinic, cooperated in the study.

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ANTHROPOMETRY IN CHILDREN

PROGRESS IN ALLERGIC CHILDREN AS SHOWN BY INCREMENTS IN HEIGHT, WEIGHT AND MATURITY

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The dramatic nature of severe allergic conditions focuses the attention of the physician and the patient on treatment of the immediate symptoms. When these have been controlled, attempts are made to learn the causes of the attack and to institute measures to prevent future symptoms. If these attempts are successful and no troublesome symptoms occur, the physician is usually satisfied with the result, despite the fact that the patient may be far from well in the sense of the fulfilment of his potentialities of health. In the adult such a result may be quite satisfactory, since, as Todd [1] has pointed out, "whatever we may do for the adult is but repair work for today." But the child is the citizen of tomorrow. His adult status will be determined by his reaction to the various influences to which he will be exposed during his period of growth and development.

That easily recognized and diagnosed illness may be of less importance than prolonged minor and often subclinical handicaps in undermining health is now recognized by all experts in child development. Todd [1] has summed up his thirty years of study of these problems as follows:

> The passage of these years has fixed in me the conviction that it is not the fully established and spectacular breakdown that destroys the happiness of living and warps a nation, but those early, unrecognized and widely spread subclinical handicaps which cripple confidence, initiative and efficiency, impair daily achievement and satisfaction, shatter ambition and cast a gray veil of uneasiness over what should be the very joy of life.

From the Asthma, Hay Fever and Allergy Foundation.

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1. Todd, T. W.: Objective Ratings of the Constitution of the Growing Child, Am. J. Dis. Child. **55**:149-159 (Jan.) 1938.

The determination of subclinical physical handicaps necessitates the application of the methods of the anthropologist to the study of patients. For clinical purposes accurate determinations of height, weight and maturity are of major importance. The technics of determining height and weight are simple. Assessment of maturity can be learned in a few months' time by careful study of roentgenograms of hands, utilizing the principles and the standards found in Todd's atlas.[2]

Graphic recording of the information obtained in various examinations of the same child at intervals will enable one to determine: (1) the status of the child when first seen, (2) the increments in each measurement at periodic intervals and (3) whether retardations are due to currently operating handicaps, to lack of compensation for earlier damage or irremediable damage in the past.

During the past several years we have been making these simple anthropometric studies of the allergic children under our care. Height and weight standards are those published by Simmons and Todd,[3] based on the studies of apparently healthy and well circumstanced children in Cleveland. Maturity standards are those of Todd.

The following case reports, with their developmental charts, are presented to illustrate the usefulness of these methods in clinical practice.

REPORT OF CASES

CASE 1.—D. M., a boy aged 9 years, had a history of infantile eczema, which cleared before 1 year of age, followed by mild rhinitis until the onset of definite, full, summer hay fever at 6 years of age. There were well marked sensitivities to grass and ragweed pollens, to the mold Alternaria and to house dust, which seemed to be of clinical importance. Despite treatment with extracts of these allergens over four years, the symptoms were not controlled completely. Physical examination revealed only the changes seen in the nose and nasopharynx usual in this type of allergy. No infection could be demonstrated.

This boy belongs to a family of short people. The mother is 5 feet (152 cm.) tall; the father, 5 feet 2 inches (157 cm.). One brother is short for his age.

A developmental examination on his ninth birthday revealed him to have the height equivalent of a boy of 8 years 7 months, a weight equivalent of 8 years 7 months and a maturity equivalent of 9 years 3 months. Evidently his constitution had not been damaged up to that time. Eight months later, at the next examination, he had progressed the equivalent of eight months in height, nine months in maturity but only four months in weight. Since there had been no illness other than the mild allergy during this interval, the failure to gain satisfactorily in weight was attributed to the allergy, and we suspected that we were seeing the earliest evidence of an effect on his constitutional health. At the next examination,

2. Todd, T. W.: The Hand, in Atlas of Skeletal Maturation, St. Louis, C. V. Mosby Company, 1937.

3. Simmons, K., and Todd, T. W.: Growth of Well Children: Analysis of Stature and Weight, Three Months to Thirteen Years, Growth **2**:93-134 (Aug.) 1938.

five months later, there were again satisfactory increments in height and maturity but a negative increment in weight, so that his weight equivalent at that time was only 8 years 9 months. This confirmed our suspicion of a fairly serious defect in constitutional health which was progressing despite our efforts to control the allergy.

Summary.—The patient had mild but continuous allergy and at 9 years of age was short but had a weight equivalent to his height and a maturity equivalent to his age; during thirteen months he achieved satisfactory increments in height and maturity but lagged in weight, so that he gained only the equivalent of two months.

CASE 2.—R. M., a brother of D. M., aged 9 years 1 month, had a history of nasal allergy since early infancy. He was a fat baby but began to grow thin at 2 years of age. Despite all the efforts of the mother and her medical advisors, the boy became progressively more asthenic in build, was a poor eater, had constant nasal symptoms and was so erratic in his conduct that a child guidance expert was consulted. He had no serious illnesses.

When seen at the age of 9 years 1 month he had the usual signs of nasal allergy without infectious complications in the sinuses.

A developmental examination at that time revealed a height equivalent of 7 years 7 months, a weight equivalent of 6 years 9 months and a developmental equivalent of 9 years 8 months. These figures represent a deficiency of eighteen months in height and twenty-six months in weight, with better than average maturity.

During a period of thirty-five months he gained in height the equivalent of twenty-three months, in weight the equivalent of thirteen months and in maturity the equivalent of only nineteen months. During this period intensive treatment for the allergy was being carried out. The clinical result, so far as control of the symptoms was concerned, was excellent. Nevertheless, this boy's constitutional health regressed, so that at 12 years of age he had a deficiency in height of thirty months, in weight of forty-eight months and in maturity of nine months.

Summary.—When first seen the patient showed a marked deficiency in height and a more marked deficiency in weight, with undisturbed maturity. He was short for his age and light for his height. As the constitutional disturbance progressed, he was further stunted in height and became lighter for his height; finally his progress in maturity was affected.

Comment.—Charts 1 and 2 illustrate progressive stages in the development of constitutional defects. When a disturbance begins it first affects increment in weight. A more severe handicap will disturb increment in height as well as that in weight. Finally, as a result of long-standing and severe damage, progress in maturity is affected.

These observations are in accord with those made on guinea pigs fed deficient diets.[4]

4. Cohen, M. B.: The Relative Ease of Interference with the Progress of Growth and Development of the Guinea Pig, Am. J. Dis. Child. **60**:636-639 (Sept.) 1940.

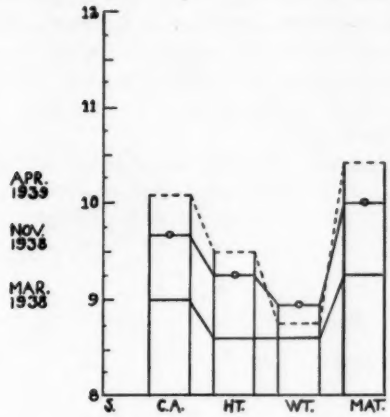

Chart 1.—Progress of D. M. in height, weight and maturity over a period of thirteen months. In this and in the subsequent charts *S* indicates standard in years; *C.A.*, chronologic age; *Ht.*, height; *Wt.*, weight, and *Mat.*, maturity.

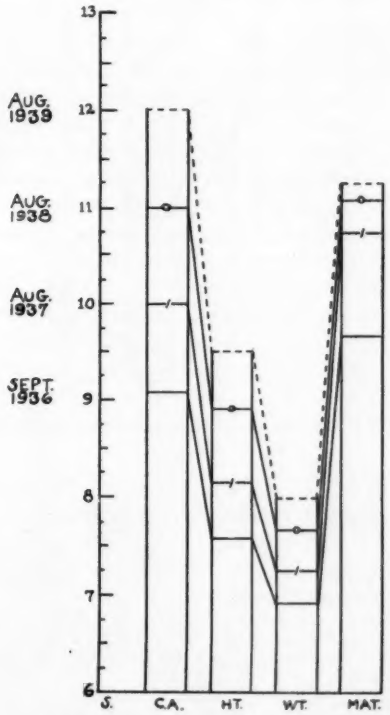

Chart 2.—Progress of R. M., in height, weight and maturity over a period of thirty-five months.

CASE 3.—M. K., a boy 11 years 9 months of age, had a history of asthma of several years' duration, which was proved to be due to the inhalation of ragweed and grass pollens, Alternaria and house dust and to the ingestion of milk.

The clinical result of treatment was unusually good. Within two weeks all symptoms were under control, and there were no significant recurrences during the time he was under our care.

At the time of his first developmental examination he had a deficiency the equivalent of fourteen months in height, thirty-three months in weight and fourteen months in maturity.

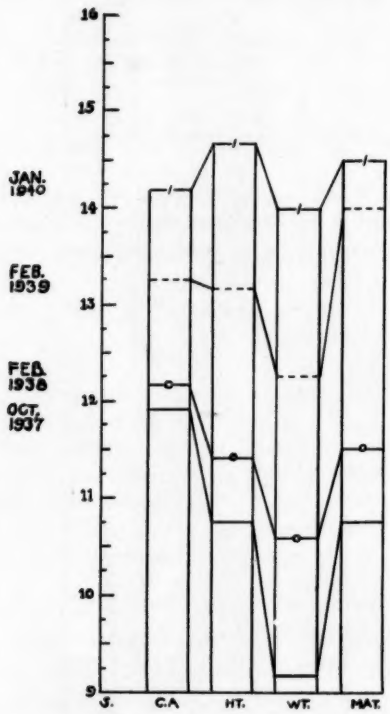

Chart 3.—Progress of M. K. in height, weight and maturity over a period of twenty-seven months.

The second developmental examination, three months later, revealed an increment in height of eight months, an increment in weight of seventeen months and an increment in maturity of nine months. Subsequent examinations revealed continued and more than adequate increments in all. Sixteen months after the beginning of treatment the deficiency in height had been completely made up, the maturity was advanced for his age and the deficiency in weight had decreased from thirty-three months to twelve months.

Eleven months later, at 14 years 2 months of age, the deficiency in weight had been made up, so that at that time this boy was up to standard in all developmental measurements.

Comment.—Chart 3 illustrates the progressive stages of recovery of constitutional vigor after severe but not irreversible constitutional damage.

The result in this boy demonstrates that the deficiencies in height, weight and maturity disclosed at the first examination were associated with the activity of his allergy and were not permanent. Progress in maturity, the most difficult to interrupt, was the first to reach the standard. This was followed by progress in height, and finally the deficiency in weight was made up.

The disturbances recorded at the first examination could not be interpreted as due to hereditary constitutional pattern, since they were overcome completely after the activity of the allergy was controlled. To compensate for deficiencies of this magnitude requires several years.

CASE 4.—J. B., a girl 13 years 1 month of age, had a history of continuous, severe and incapacitating allergy since infancy. Gastrointestinal symptoms began at 3 weeks of age and were soon followed by severe eczema. Nasal symptoms began at 4 months of age and asthma at 6 months. The child grew erratically and by 6 years of age had a well marked pigeon breast deformity with beginning organic emphysema. Because of her constant ill health she was four years behind in school.

Physical examination at the age of 13 years 1 month revealed a frightened, shy girl, difficult to manage, with the general appearance of a thin child of 6 or 7 years of age. The face was small, with flat malar prominences; the palate was narrow and high arched. She was having an asthmatic attack of moderate severity. There was well marked emphysema, with a barrel-shaped deformity of the chest, complicated by an earlier pigeon breast deformity. Asthenia was marked.

Cutaneous tests revealed sensitiveness to so many food and inhalant allergens that it was difficult to determine the clinical sensitiveness. After many months of clinical observation it was found that symptoms could be produced by exposure to ragweed and grass pollens, animal danders, house dust, cottonseed and several foods. Avoidance of these foods and animal danders, cottonseed and house dust, together with attempts to increase her tolerance to the pollens and dust, was followed by considerable improvement in her symptoms. The acute asthmatic attacks became infrequent, but she was never free of some wheezing. There was a remarkable psychologic improvement. She was able to attend school regularly and made good progress.

Anthropometric examination at the age of 13 years 1 month revealed a height equivalent of 8 years 8 months, a weight equivalent of 5 years 11 months and a maturity equivalent of 9 years 3 months or a deficiency for her age of fifty-two months in height, eighty-six months in weight and forty-six months in maturity. At the next examination, seven months later, there had been no increase in height and a small loss in weight, but the maturity had increased by the equivalent of thirteen months. At the examination ten months later both height and weight had increased by small increments; the increment in maturity was more than adequate. On her seventeenth birthday, forty-seven months after the original examination, she had increased in height by the equivalent of thirty-four months, in weight by the equivalent of thirty-three months and in maturity by the equivalent of forty-eight months. She is still markedly retarded.

Comment.—Chart 4 illustrates partial recovery from a severe constitutional handicap associated with continuous and long-standing allergy as the retarding effects of the active disease were partially removed. It is worthy of note that progress in maturity was the first to appear,

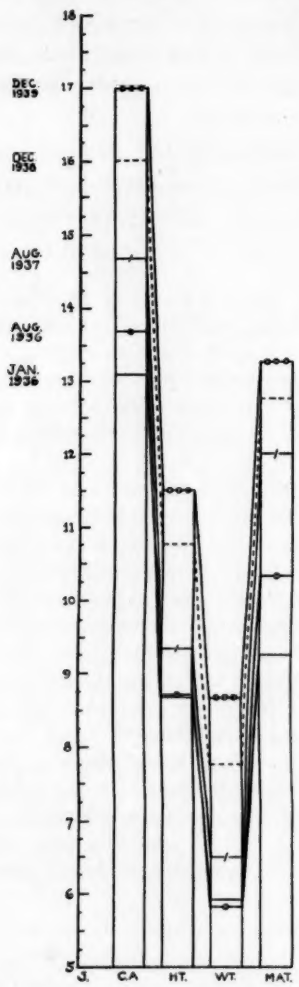

Chart 4.—Progress of J. B. in height, weight and maturity over a period of forty-seven months.

followed in seventeen months by the first increase in height and weight. After seventeen months there was a regular and fairly normal increase in all three measurements.

In this case the constitutional damage had both reversible and irreversible components. The gains represent the ability of this child to

develop regularly after the major handicap was removed. Failure to make up any of the deficiency, however, indicates marked and probably permanent constitutional damage.

Fortunately there are patients with allergy in whom no constitutional damage can be demonstrated. These are not necessarily the the ones with trivial symptoms. Just as the severity of symptoms for a given exposure to an allergen depends on the reactivity of the person exposed to it, so does the degree of constitutional disturbance. Clinical observation indicates that simple hay fever alone seldom affects the growth pattern. Mild and often subclinical upsets mediated through the gastrointestinal tract are more likely to do so.

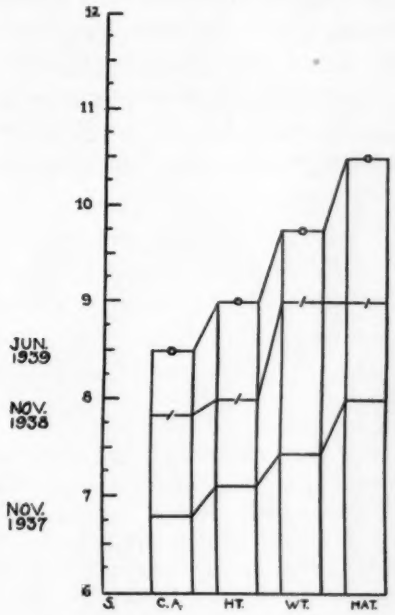

Chart 5.—Progress of A. S. in height, weight and maturity over a period of twenty months.

Case 5.—A. S., a girl 6 years 10 months of age, had had attacks of nasal stuffiness and wheezing, accompanied by nausea and vomiting, at periodic intervals since 1 year of age. She had hives from the ingestion of chocolate, rhubarb and strawberries. Eggs caused vomiting. The nasal and bronchial symptoms were controlled by eliminating the major contacts with dust and by treatment with house dust and ragweed extracts.

Her first developmental examination, at the age of 6 years 10 months, revealed a height equivalent of 7 years 2 months, a weight equivalent of 7 years 5 months and a maturity equivalent of 8 years. Subsequent examinations revealed satisfactory increments in all measurements, so that at 8 years 6 months of age she had a height equivalent of 9 years, a weight equivalent of 9 years 9 months and a maturity equivalent of 10 years 6 months.

Comment.—Despite an active allergy of moderate severity during late infancy and early childhood, the child had no disturbance of her growth pattern. In fact, she was advanced for her age in growth and development.

COMMENT

These case reports illustrate the value of anthropometry in recording progress in allergic children. Allergy is only one of many conditions which may disturb the growth pattern. When careful study enables one to rule out conditions other than allergy, the developmental progress of a child can be used to determine the efficacy of the treatment of the allergy. Graphic records, as illustrated here, enable the clinician to pick out those children who are lagging in their development. No child can be considered healthy who fails to achieve suitable and regular increments in height, weight and maturity. Careful clinical study of the children who are lagging in development will usually disclose some chronic handicap, the removal of which will be followed by improvement in the developmental pattern and often by complete compensation.

RELATION OF SEPSIS TO INFECTIONS OF THE UPPER RESPIRATORY TRACT

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In this paper we are presenting a study of 70 patients with sepsis associated with infections of the upper respiratory tract: cervical adenitis, sinus thrombosis and inflammation of the accessory nasal sinuses. All of them had acute pharyngitis; a small number had pharyngitis as the sole complication. We studied the effect these foci exercised on the course of the sepsis. We also considered the effect of sepsis on these complications of acute pharyngitis. The 70 patients were part of a series of 320 children with sepsis of all types.

Blood culture studies were made for all patients with fever admitted to the pediatric wards between 1931 and 1935. The blood cultures were made according to standard methods by an intern assigned to the service. All the work was supervised by one person, insuring a good degree of uniformity in results throughout the years during which these cultures were made.

Fourteen cubic centimeters of the patient's blood was drawn and poured into culture mediums at the bedside. Five cubic centimeters was injected into each of two 200 cc. Erlenmeyer flasks. The first flask contained 125 cc. of veal infusion broth at p_H 7.2; the second flask contained 125 cc. of 2 per cent dextrose veal infusion broth of the same hydrogen ion concentration. The remaining 4 cc. of blood was divided equally to form two pour plates, one with a 2 per cent dextrose veal infusion agar and the other with a tube of plain veal infusion agar. Daily transplants were made from the two flasks, and smears were stained at the same time. Organisms were identified by cultural and serologic methods. Every gram-positive coccus, except the staphylococcus, was subjected to the bile solubility test and to agglutination with the specific types of antipneumococcus serums. For gram-negative bacilli, the standard sugar reactions and serologic methods were used.

SEPSIS AND CERVICAL ADENITIS

We studied 57 patients with cervical adenitis. Twenty-four had positive blood cultures while 33 had sterile cultures. The 24 patients with positive cultures represented 7 per cent of a total of 320 patients with all types of sepsis. Patients included in this series had definite

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enlargement of the lymph nodes. There was in most instances a matting of the lymph nodes and skin to form a mass which required incision and drainage. We did not include cases in which the glands were described as "slightly enlarged," or "shotty" or "palpable" or those in which there was generalized adenopathy. That the presence of bacteremia did not depend on whether the culture was made early or later in the course of the illness is shown in chart 1.

Bacteria.—Of the 24 patients with positive blood cultures, 82 per cent had an invasion with Streptococcus haemolyticus, 8 per cent with Streptococcus viridans, 8 per cent with Pneumococcus and 3 per cent with Staphylococcus. The invasion was large in 40 per cent, medium in 25 per cent, small in 30 per cent and of unknown size in 8 per cent of the patients.

Age.—Age was an important factor in determining the incidence of sepsis in patients with cervical adenitis. The greatest incidence occurred in the group of patients under 1 year of age. Fifty per cent of the patients

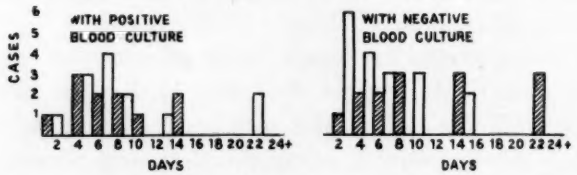

Chart 1.—The day of illness on which patients with cervical adenitis were admitted.

with adenitis in the 1 to 5 year age group had sepsis. It developed three times as often in the children under 1 year of age as in those in the 1 to 5 year group. On the other hand, patients with cervical adenitis who were over 5 years of age had sepsis only one sixth as often.

Sex.—In two thirds of the girls with cervical adenitis sepsis developed, whereas this complication appeared in only one half of the boys.

Tonsillectomy.—Among the 57 patients with cervical adenitis, 13 had previously had tonsillectomy. Of these 13, sepsis developed in only 1, and this child had had regrowth of some of his tonsillar tissue. It seems that although tonsillectomy does not prevent adenitis in a child, it does greatly diminish the chance of the complication of adenitis by sepsis.

Morbidity.—The duration of illness was about the same in the patients with positive and in those with negative blood cultures. However, the patients with positive blood cultures had twice as many secondary local-

izations, and these were preponderantly outside the respiratory tract. In those with sterile blood cultures most of the secondary foci were within this tract. These facts are summarized in the table and in chart 2.

Mortality.—The onset of sepsis in a patient with cervical adenitis adversely affects the prognosis, since the mortality without sepsis is 3 per cent, whereas a complicating sepsis raises the death rate to 63 per cent. Moreover, the mortality in patients with sepsis associated

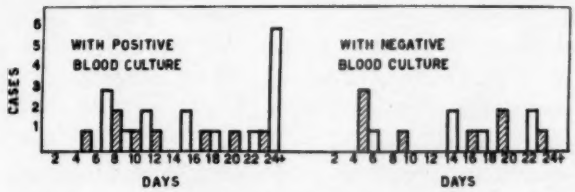

Chart 2.—Duration of acute illness in patients with cervical adenitis.

Distribution of Associated Localizations in Patients with Cervical Adenitis

Distant Localizations	Patients with Positive Blood Cultures	Patients with Negative Blood Cultures
Skin		
Erysipelas	4	1
Other cutaneous lesions	6	5
Peritonitis	5	0
Kidney (hemorrhagic nephritis only; no patients with focal lesions)	0	3
Gastrointestinal tract	0	0
Osseous involvement	3	0
Questionable involvement of bone or soft tissue	3	0
Meningitis	1	0
Stomatitis	1	0
Total	23	9
Localizations in Respiratory Tract		
Retropharyngeal abscess	6	8
Pharyngeal edema	0	6
Mastoid	2	0
Sinus thrombosis	1	0
Sinusitis	2	2
Ears	8	18
Lungs	7	8
Empyema	5	1
Total	31	43

with cervical adenitis is greater than in those with other forms of sepsis. In a series of our patients (142) with streptococcemia of all types, the mortality was 56 per cent, as against that of 63 per cent in those patients in whom streptococcemia was associated with adenitis.

SEPSIS AND MASTOIDITIS WITH SINUS THROMBOSIS

Bacteria.—In the series of patients studied there were 39 for whom a diagnosis of sinus thrombosis was made and was confirmed at operation. These were all patients in whom the sinus thrombosis was

otitic in origin. We are not concerned with the infantile type of thrombosis, recently described by Bailey and Hass.[1] We found a demonstrable sepsis in 77 per cent of patients with sinus thrombosis. The incidence of positive blood cultures as reported by different clinics varies tremendously: Kopetzky[2] reported 42 per cent positive; Juers,[3] 61 per cent; and Meltzer,[4] in a series from the Massachusets General Hospital, 25 per cent. On the other hand, Friesner[5] reported an incidence of 90 per cent of positive blood cultures, and Goldman and Shwartzman[6] reported 96 per cent positives among patients of the Mount Sinai Hospital of New York. We are inclined to agree with Goldman and Shwartzman that positive blood cultures can be obtained for a high percentage of patients with sinus thrombosis. The incidence of positive cultures will depend to a great extent on the amount of blood cultured, on the sensitivity and variety of the mediums employed and on the amount of care used. The frequency of positive blood cultures depends especially on the quality of the liquid mediums. Goldman and Shwartzman have shown that the use of a vitamin broth gives the best results. In their series of cases the percentage of positive cultures on solid mediums was about the same as in ours, whereas their incidence of positive cultures in the broth was much higher than ours (50 per cent of their cases). There may be, as many authors claim,[7] thrombi which are really sterile, but such occurrences must be few.

The organism in all of our cases was Str. haemolyticus. Of the 30 patients with positive blood cultures, 22 had large invasions, 3 had medium invasions and 4 had small invasions.

While a negative culture does not rule out sinus thrombosis, does a positive culture in the presence of an infection of the ear necessarily indicate sinus thrombosis? It is our opinion that even the smallest

1. Bailey, O. T., and Hass, G. M.: Dural Sinus Thrombosis in Early Life: The Clinical Manifestations and Extent of Brain Injury in Acute Sinus Thrombosis, J. Pediat. **11**:755 (Dec.) 1937.

2. Kopetzky, S. J.: Studies in Otitic Sepsis, Ann. Otol., Rhin. & Laryng. **37**:329 (March) 1928.

3. Juers, A. J.: Otitic Sepsis: Analysis of Twenty-One Cases and Anatomic Study, Arch. Otolaryng. **27**:178 (Jan.) 1938.

4. Meltzer, P. E.: Treatment of Thrombosis of the Lateral Sinus, Arch. Otolaryng. **22**:131 (Sept.) 1935.

5. Friesner, I.: Infections of the Middle Ear, Arch. Otolaryng. **14**:257 (Sept.) 1931.

6. Goldman, J. L., and Shwartzman, G.: Streptococcus Hemolyticus Bacteremia, with Special Reference to Otolaryngologic Conditions, Ann. Otol., Rhin. & Laryng. **44**:961 (May) 1935.

7. Dean, L. W., and others: Panel Discussion: Septic Thrombophlebitis of the Sigmoid Sinus, Tr. Am. Acad. Ophth. **42**:402, 1937.

degree of invasion of the blood stream in the patient with otitis media or mastoiditis probably indicates a complicating sinus thrombosis. During the period when our patients with sinus thrombosis were being studied, we also observed a series of 60 patients with acute mastoiditis. None of them had positive blood cultures. This is in accord with the experience of Friesner,[5] who also has expressed the belief that mastoiditis in itself does not produce bacteremia. We found untenable the theory of Körner that there can be an osteophlebitis in mastoiditis which is responsible for sepsis.

Of course, all nonotitic sources of sepsis must be excluded. Thus, a patient with otitis or mastoiditis may suffer bacteremia from concomitant pharyngitis, from early, undiagnosed pneumonia or from endocarditis. Such possibilities may be ruled out by careful clinical observation and by repeated blood cultures. The bacteremia accompanying acute pharyngitis or early pneumonia is usual a small, transitory invasion.

In the majority of cases of sinus thrombosis, although the earliest cultures show a small invasion, the bacteremia quickly assumes a persistent character, with an increasing number of colonies per cubic centimeter of blood. We had 13 patients for whom repeated blood cultures were made before operation. The blood of 7 patients showed a definitely increasing invasion (from medium to large in 5 and from small to large in 2). The blood of 1 patient showed an increase from a medium to a large invasion and then became sterile before operation. There were also exceptions to this trend. There were 4 patients whose blood became sterile before operation. In 2 others whose blood showed decreasing invasions localization had developed in joints before operation to account for the diminution in the invasion.

Age.—Sinus thrombosis occurs chiefly during the early school age. Sixty-six per cent of the children affected were from 5 to 9 years old, and 90 per cent of the total group were from 5 to 12 years of age. Boys and girls were equally affected.

Season.—By far the highest incidence occurred during the spring.

The Year by Year Distribution of Cases.—We found that the year by year incidence of sinus thrombosis remained fairly constant throughout the six year period.

Incidence of Tonsillectomy.—Thirty-one of the patients (80 per cent) had had tonsillectomy previous to their illness. We therefore felt that tonsillectomy had no influence on the incidence of sinus thrombosis in mastoiditis.

Localizations.—In the 30 patients with sinus thrombosis whose blood cultures were positive there was a total of forty additional localizations. These were distributed as follows:

Bones and joints	13
Skin	
Abscesses	0
Petechiae	0
Purpura	1
Erythema	1
Kidneys	3
Central nervous system	
Hemiplegia	1
Sterile meningitis	1
Delirium	2
Gastrointestinal system	
Peritonitis	1
Abdominal pain	1
Lungs	7
Empyema	1
Upper respiratory tract	
Other ear	6
Cervical adenitis	1
Labyrinthitis	1

In the 9 patients who did not have positive blood cultures, there were no distant localizations. There seemed, however, to be a greater degree of extension locally:

Other ear involved	4
Other mastoid involved	2
Peritonsillar abscess	2
Adenitis	1
Subdural abscess	1

Effect of Operation on Septicemia.—One of the most interesting problems was the effectiveness of the operative procedure in sterilizing the blood. In our service the operation usually consisted of exposing the sinus along its entire length until normal tissue was reached. The thrombus was then removed and the ends of the sinus blocked off. The jugular vein was tied off at the same time or a day later.

All the patients were operated on. The blood of 10 patients became sterile within twenty-four hours. Sterile cultures were obtained for 4 additional patients within three days after operation. On the other hand, 10 patients continued to show organisms in the blood after the third day. For less than 50 per cent of the patients, therefore, sterile

blood cultures were obtained within the first three days after operation. In addition to the patients already enumerated, there were 3 who had positive blood cultures on admission which became sterile spontaneously before operation. There were 2 patients who showed organisms in the blood for the first time postoperatively.

The 2 patients for whom positive blood cultures were obtained for the first time after operation were of more than usual interest. The explanation that occurred to us was that the bacteremia might be due to trauma from the operative intervention. Inadequacy of the technic of making the blood culture, however, seems a more likely possibility. In the following section it is pointed out that a great many of the distant localizations, though planted before operation, do not develop until after operation and that secondary bacteremias from these new foci are often heavier than the invasions of the blood stream from the original sinus thrombosis. A technic that is good enough to isolate the heavier invasion due to a secondary focus might not be sufficient to detect the small bacteremia from an early thrombosis. The results in the various series of cases reported substantiate this: The higher the percentage of preoperatively positive cultures, the smaller the number of new, postoperatively positive cultures. In Meltzer's series, in which only 25 per cent of the patients had a preoperatively positive blood culture, a positive culture was obtained for the first time after operation for 20 per cent. In our series in which 77 per cent of the patients had preoperatively positive cultures, a positive culture was obtained for the first time after operation for only 7 per cent. In the series of Goldman and Shwartzman, in which 96 per cent of the preoperative cultures were positive, there were no patients for whom a positive blood culture was obtained for the first time after operation.

Effect of Operation on the Incidence of Subsequent Foci.—It is a well established fact that peripheral foci add to the critical nature of sinus thrombosis. Meltzer [4] and others have pointed out that operation does not minimize the incidence of distant localization. In fact, in Meltzer's reports it was shown that there were four times as many localizations after ligation of the jugular vein as before.

Of the 30 patients with positive blood cultures, suppurative foci developed in 11 subsequent to the operation. These foci, of course, may have developed from emboli planted previous to the operation and may explain the high incidence of postoperatively positive blood cultures. Nine of these 11 patients had positive blood cultures after operation, and they were included in the group of 12 who continued to have postoperative sepsis. Even if the foci are a result of previously planted emboli and persistence of the sepsis is due to these secondary foci, the operation is still of utmost importance, as it closes off the original source of infection.

Morbidity.—Our study is concerned only with the duration of acute symptoms after operation. The facts are set forth in chart 3.

As a general rule the patient who has postoperative sepsis or in whom a focus develops postoperatively or one in whom both these occurrences supervene will have a longer period of illness. The exceptions to this rule, however, can be striking, for the 2 patients with the longest morbidity in the group had neither persistent sepsis nor new foci following operation.

Mortality.—Five of the patients with positive cultures (17 per cent) and 1 with a sterile blood culture (11 per cent) died, making an average mortality of 15 per cent. In Evans' series [8] of 979 cases collected from different sources, there was a mortality of 31.2 per cent. He cited Lillie's report, which gives a death rate of only 9.8 per cent in the cases reported from the Mayo Clinic.[8a]

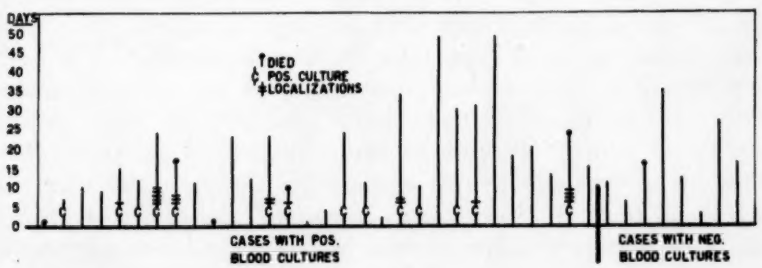

Chart 3.—Duration of acute symptoms in patients with sinus thrombosis after operation.

The cause of death was not always the sepsis itself. One child who died of uremia had been admitted for chronic nephritis several times before. In 1 patient an abscess of the brain developed, with hemiplegia; another died because of a localization in the peritoneum, and in another, with repeatedly negative blood cultures, a subdural abscess developed by direct extension, from which he died. The clinical picture presented by the fifth patient who died was marked by the development of severe delirium.

In all 5 deep subcutaneous foci developed about the small joints of the hands and feet, none of which suppurated. This is contrary to the experience of Kopetzky,[2] who found that deep subcutaneous foci meant a favorable outcome.

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8. Evans, W. H.: Thrombosis of the Lateral Sinus: Survey of Current Opinion and Records, Arch. Otolaryng. **28**:959 (Dec.) 1938.

8a. Sutherland, J. M.: Otitic Sinus Thrombosis, Arch. Otolaryng. **27**:1 (Jan.) 1938.

SEPSIS AND INFLAMMATION OF THE ACCESSORY NASAL SINUSES

In our series of 320 patients with sepsis, 7 (2 per cent) had associated sinusitis. The number is too small for a complete statistical study, so that only a brief outline of the available facts is given.

Of these 7 patients there were 5 (group 1) in whom sinusitis was the sole or most important localization, and in 2 (group 2) the importance of the sinusitis was overshadowed by that of associated (or other) localizations. The left ethmoid sinus was involved in 6 patients and the left antrum in 1. In 2 of the patients there was also involvement of the other sinuses.

Bacteria.—The organism in the blood stream in these patients was Str. haemolyticus in 5 and Str. viridans in 2.

In all cases the results of the bacterial study of the pus evacuated from the sinus agreed with those from study of the blood.

Age.—Three of the patients were under 2 years of age, and 4 were from 5 to 8 years of age.

Mortality.—Three of the patients died. One was from group 1 and 2 were from group 2.

During the same period we observed 21 patients with sinusitis whose blood cultures, obtained by the same methods, were negative. In 15 of these sinusitis was the only clinical condition. In 7 there was associated pneumonia or bronchitis. The condition of 2 of the patients necessitated radical operative intervention; the others were treated conservatively. Six of the patients showed swelling of the lids and various degrees of ocular proptosis, indicating retrobulbar cellulitis. The incidence by age group was as follows: under 2 years, 3 patients; 3 to 8 years, 6, and over 8 years, 12.

The literature on the subject of sinusitis and septicemia is sparse. In a report by Goldman,[9] 71 patients with sinusitis are cited for whom blood cultures had been made. Sixteen, or 23 per cent, of the cultures were positive. All the positive cultures, however, were for the patients who had one complication or another: orbital cellulitis, orbital abscess, osteomyelitis of the skull, acute purulent meningitis, abscess of the brain, cavernous sinus thrombosis, sympathetic meningitis, meningomyeloencephalitis or temporal edema.

Of course, a focus for the streptococcemia other than the sinuses must be considered. In group 1, 1 patient had complicating osteomyelitis of the palate. In the other 4 patients, however, we feel that the course of events justifies the opinion that the uncomplicated sinusitis itself was the focus for the septicemia. Recent work tends to con-

9. Goldman, J. L.: Complications of Acute Sinusitis, with Special Reference to Bacteremias, Laryngoscope **46**:500 (May) 1936.

firm our opinions. Larsell and associates[10] reported experimental evidence which indicates that the lungs and blood of dogs may be invaded from the sinuses without the occurrence of osteomyelitis.

ROLE OF ACUTE PHARYNGITIS IN THE SEPTICEMIAS OF CHILDHOOD

The frequent association of acute pharyngitis with sepsis in childhood is well known. In our series of 320 patients with sepsis of all types, 226, or 71 per cent, had associated sore throat. The incidence of sore throat, though high in all forms of sepsis, does vary with the organism concerned. The frequent association of pharyngitis with streptococcemia and pneumococcemia is well known, but the association of pharyngitis with staphylococcemia and sepsis from Bacillus coli has not been sufficiently stressed.

The skin is usually considered the portal of entry in staphylococcic sepsis. All our patients also had cutaneous lesions that may have been the primary foci. Infections and abrasions of the skin, however, are ubiquitous, and even when found one still has to explain why in a particular case bacterial invasion of the blood should have resulted. We have noted that many of our patients with staphylococcemia also had pharyngitis. It may be that the immunologic changes effected by the onset of pharyngitis can convert an innocuous lesion into a focus of infection, just as an attack of influenza can make possible invasion of the lung by hitherto nonpathogenic staphylococci.

Although pharyngitis is so frequent in all types of sepsis, it rarely is the sole complication. Of our 320 patients, only 9, or 3 per cent, had pharyngitis as the only clinical manifestation besides the positive blood culture. We have been greatly interested in the relation of pharyngitis to sepsis. As an approach to the problem, we have tentatively classified sore throat in accordance with its severity as follows:

1. Severe pharyngitis (pharyngitis predominating). In this type, at the time bacteremia is found the throat is acutely and severely inflamed, with the pharyngeal wall and the tonsillar fauces markedly congested and red.

2. Mild pharyngitis (pharyngitis nonpredominating). In patients with this type, pharyngitis is also present at the time the blood culture is found to be positive, but the throat, though diffusely red, does not appear angry or severely inflamed.

The appearance of sore throat did not depend on the time of admission to the hospital. Of the patients with pharyngitis predominating, 30.7 per cent were admitted before the fourth day of illness and 66.5

10. Larsell, O.; Veazie, L., and Fenton, R. A.: Streptococcic Infections of the Lungs from the Paranasal Sinuses: Experimental Study, Arch. Otolaryng. **27**:143 (Feb.) 1938.

per cent before the seventh day of illness. Of the patients with non-predominating pharyngitis, 33.5 per cent were admitted before the fourth day of illness and 65 per cent before the seventh day.

The possible significance of this grouping can best be illustrated by a study of the relation of the type of pharyngitis to the prognosis in sepsis. Chart 4 shows that the mortality is markedly and consistently

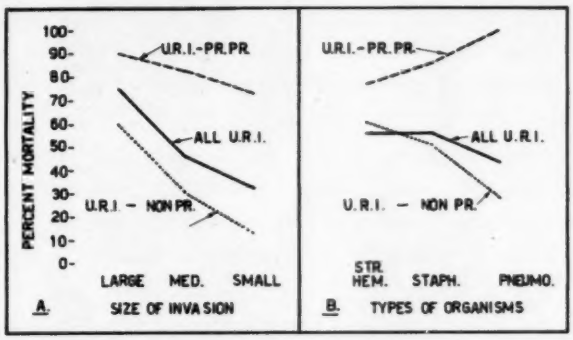

Chart 4.—Percentage of mortality in cases of sepsis accompanied by either type of pharyngitis: *A*, according to size of invasion; *B*, according to organism. In this and in subsequent charts *U.R.I.* indicates upper respiratory infection; *PR. PR.*, predominating pharyngitis; *NON PR.*, nonpredominating pharyngitis.

AGE GROUP	0-1yr	1-2	2-3	3-5	5-9	9-12
NO. PTS. IN GR.	124	36	28	25	67	40
NO. Σ PR.N. PR.	70	21	15	12	44	18
NO. Σ PR.PR.	13	14	9	2	4	4

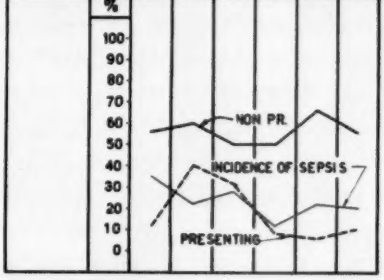

Chart 5.—Incidence according to age of both types of pharyngitis in patients with sepsis.

increased in those patients with predominating pharyngitis, regardless of the type of organism or the magnitude of invasion. The mortality in patients with sepsis with a small invasion who had predominating pharyngitis was 72 per cent. While the mortality in patients with pneumococcemia is lower than that in patients with streptococcemia, those with pneumococcic sepsis who had predominating pharyngitis suffered a mortality of 100 per cent.

The interrelation of age, prognosis and severity of pharyngitis is also interesting. As can be seen in chart 5, the incidence of sepsis decreases with increasing age. With the sepsis that does occur in the older age group, the incidence of predominating pharyngitis decreases, but the percentile incidence of nonpredominating pharyngitis remains as high in the older patients with sepsis as in the infants. We have found that not only is the incidence of sepsis lower in the older children but the mortality is less. Chart 6 shows that this is true only because the number of patients with predominating pharyngitis becomes smaller in the older age group.

The incidence of these two types of pharyngitis in patients with the different types of sepsis is also interesting. Generally, if those with all the types of sepsis are grouped together, there are four times as many with nonpredominating pharyngitis as there are with the predominating type of pharyngitis. The ratio, however, does vary to some extent with the type of sepsis. The proportion in patients with streptococcic sepsis remains 4:1; in those with pneumococcemia the ratio is increased to 6:1 while in those with staphylococcemia it drops to less than 2:1 (chart *7 A*). If all the patients are grouped together, the proportion of those with nonpredominating to those with predominating pharyngitis remains 4:1 no matter how large or small the invasion (chart *7 B*). However, if the relation of the size of invasion to the type of pharyngitis is examined for each organism, there is a significant variation. In persons with streptococcemia and staphylococcemia associated with nonpredominating pharyngitis, the incidence of large invasions is markedly greater than that of the medium or small invasions (chart *7 D*). When these two types of sepsis are associated with predominating types of pharyngitis, the proportion of large invasions equals that of the small invasions (chart *7 C*).

With regard to pneumococcemia, the reverse holds true. When pneumococcemia is associated with the nonpredominating types of pharyngitis, the small invasions predominate, and the percentile incidence of patients with large invasions drops (chart *7 D*). When the pneumococcic sepsis is associated with the predominating type of pharyngitis, however, the percentage of large invasions is overwhelmingly greater than that of the small invasions (chart *7 C*). Stated differently, many more patients with streptococcemia and staphylococcemia have large invasions than have small ones. This preponderance is even greater in those with nonpredominating pharyngitis. However, few patients with pneumococcemia have large invasions; and of these few all have a predominating type of pharyngitis.

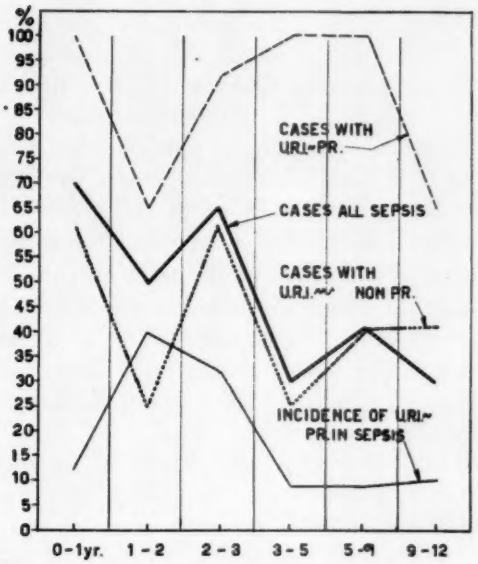

Chart 6.—The mortality of patients with sepsis in different age groups with each type of pharyngitis.

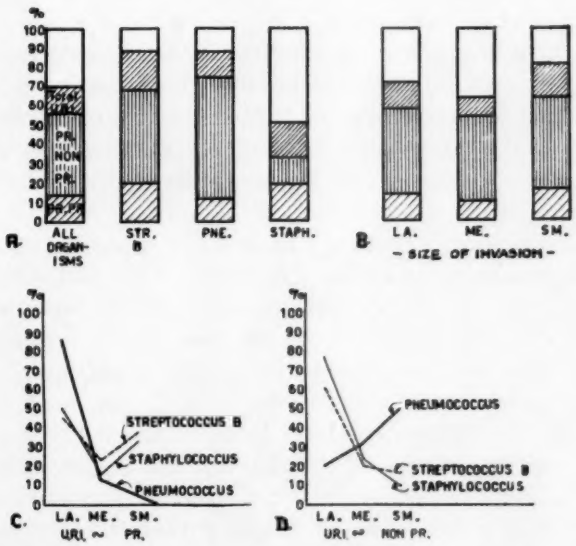

Chart 7.—Relation of pharyngitis to septicemia: *A*, incidence of each type of pharyngitis in streptococcemia, pneumococcemia and staphylococcemia; *B*, relation of type of pharyngitis to size of bacterial invasion, *LA.* indicating large, *ME.*, medium, and *SM.*, small; *C*, incidence of predominating pharyngitis in patients with different sizes of bacterial invasion; *D*, incidence of nonpredominating pharyngitis in patients with different sizes of bacterial invasion.

COMMENT AND SUMMARY

Seventy patients in whom sepsis was closely associated with lesions of the throat, cervical glands, mastoid and nasal sinuses were studied. These included 9 patients with pharyngitis, 24 with cervical adenitis, 30 with sinus thrombosis and 7 with inflammation of the accessory nasal sinuses. These 70 patients were part of a series of 320 children with septicemia of all types. The clinical course in these 70 cases and the bacteriologic data are compared with those observed in a larger series of patients with sepsis and with those found in patients with the same clinical condition who had sterile blood cultures.

The factors that determine prognosis in sepsis are evaluated. The presence of severe pharyngitis was found to be a bad prognostic sign, while mild pharyngitis indicated a relatively better outlook. These facts provide a basis for estimating the effect of chemotherapeutic agents in the treatment of sepsis.

Sepsis occurs frequently with some lesions of the upper respiratory tract and infrequently with others. Mastoiditis alone, simple pharyngitis or uncomplicated sinusitis is seldom accompanied by sepsis. This fact is of diagnostic importance. Persistent bacteremia in a patient in the presence of definite mastoiditis has, in our experience, always indicated the presence of sinus thrombosis. On the other hand, a negative blood culture associated with such a condition speaks against the presence of sinus thrombosis.

The influence of previous tonsillectomy in determining the incidence of sepsis varies with the nature of the focus. It appears that previous tonsillectomy reduces the chance of the complication of cervical adenitis by sepsis. On the other hand, many of our patients with mastoiditis in whom sinus thrombosis and sepsis developed had previously had tonsillectomy.

Much experimental evidence is needed to explain the essential differences between severe and mild pharyngitis. Our first differentiation of pharyngitis into two types was tentative, but we were encouraged to follow it through when we observed how the classification seemed to divide patients into two groups with regard to prognosis, morbidity, size of invasion and type of organism. We do not know the reason for the correlation between prognosis in sepsis and the type of pharyngitis. The exposed position of the pharynx and the presence there of pathogens in most persons makes it a possible focus for numerous organisms. At the same time, it is not unlikely that systemic infections may modify the appearance of the pharynx and that this may in some way be related to the severity of the disease. To substantiate this, we need only bear in mind the pharyngitis of scarlet fever and of measles and perhaps also the pharyngeal changes in such diseases as leukemia and granulocytopenia.

We discovered some interesting data regarding pneumococcic sepsis. There seem to be two different types of pneumococcemia. In the first, the more frequent of the two, the patient is admitted with the signs and symptoms of pneumonia. He has pharyngitis, but it is mild. Blood culture reveals pneumococcic bacteremia, but this invasion of the blood stream is small and transient. In the second type, the picture is that of severe septicemia with a large and persistent invasion and an invariably fatal outcome. Pharyngitis is generally severe at the time bacteremia occurs. This type of pneumococcemia is usually associated with the end stage of prolonged pneumonia, with peritonitis, meningitis or, more rarely, with osteomyelitis.

The blood of 10 patients with sinus thrombosis became sterile within twenty-four hours after operation and of 4 within three days, while that of 10 patients continued to show organisms for more than three days after operation. The blood of 3 of the patients became sterile even before operation and that of 2 became positive for the first time after operation. In 11 patients new suppurative foci developed after operation. Of these, 9 were in the group of those who had persistently positive blood cultures postoperatively.

OBESITY IN CHILDHOOD

IV. ENERGY EXPENDITURE OF OBESE CHILDREN

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Excessive deposition of fat and abnormal increase in weight presuppose that the organism receives more food than it burns under the given circumstances of its life. The problem of food intake of obese children has been dealt with in a previous paper.[1] It was found that the food intake of most obese children was far in excess of that of nonobese children. In many cases the food intake was so large that it might well have accounted for the progressive increase in weight. The problem arises as to whether conservation in energy expenditure of obese children is another factor contributing to the excessive accumulation and storage of fat tissue.

Energy is derived from the food ingested. The utilization of food by obese persons is not different from that by thin persons,[2] and the correction for nonresorbed food is similar in both instances. In contrast to this single source of energy intake, there are several ways in which energy is expended. This paper will deal only briefly with those aspects of energy expenditure which are represented by basal metabolism, requirements for growth and specific dynamic action of food. The main object of the report will be an inquiry into the physical activities of obese children, which will be discussed in their quantitative aspects, in their relation to the development of obesity and in their psychologic significance.

BASAL METABOLISM

Basal metabolism designates the energy expenditure of the resting and fasting organism. The assumption that the basal metabolic needs of obese persons are lower than normal led to the theory that hypothyroidism was a cause of adiposity. This problem was discussed in detail in a

This investigation has been aided by a grant from the Josiah Macy Jr. Foundation.

From the Department of Pediatrics, College of Physicians and Surgeons, Columbia University, the Pediatric Division of the Vanderbilt Clinic and the Babies Hospital.

1. Bruch, H.: Obesity in Childhood: III. The Food Intake of Obese Children; Physiologic and Psychologic Aspects, Am. J. Dis. Child. **59**:739 (April) 1940.

2. Neuenschwander-Lemmer, N.: Ueber Ausnutzungsversuche bei fettsüchtigen und normalen Menschen, Ztschr. f. d. ges. exper. Med. **99**:394, 1936.

previous paper.[3] Numerous observations have conclusively demonstrated that obese persons have basal metabolic requirements which equal or surpass those of normal subjects of the same height or age. Hence obesity cannot be explained on the basis of low requirements for the basal metabolism.

REQUIREMENTS OF GROWTH

It is obvious that a rapidly growing child requires proportionally more energy per unit of body substance than a slowly growing child or an adult. Exact information concerning these requirements can be obtained only by longitudinal observations on a group of children in different phases of growth. I am not familiar with any study which has presented such accumulated observations on comparable groups of obese and normal children. The fact, however, that obese children grow and mature at a rate faster than normal [4] militates against the assumption that their energy requirements for growth are less than those of nonobese children.

SPECIFIC DYNAMIC ACTION OF FOOD

The term specific dynamic action refers to the increase in metabolism after food intake; this increase is higher for protein than for carbohydrate or fat.[5] In 1922 Plaut [6] described the differences between normal and obese persons in metabolic response to food intake. She observed that certain obese patients, whom she described as showing "hypophysial obesity" (without giving any evidence as to the validity of this diagnosis), reacted to the ingestion of food with an increase in heat production that was markedly lower than that observed in normal persons. From these and other observations she deduced that pituitary disturbances are characterized by a low specific dynamic action. Since in her observation patients with so-called constitutional obesity behaved in a similar way after ingestion of food, she also drew the conclusion that most cases of obesity are of hypopituitary origin. Many papers which corroborated the findings and conclusions of Plaut are characterized by a similar laxity in diagnosis and reasoning. Workers who restricted their observations to patients with definite abnormalities of the hypophysis failed

3. Bruch, H.: Obesity in Childhood: II. Basal Metabolism and Serum Cholesterol of Obese Children, Am. J. Dis. Child. **58**:1001 (Nov.) 1939.

4. Bruch, H.: Obesity in Childhood: I. Physical Growth and Development of Obese Children, Am. J. Dis. Child. **58**:457 (Sept.) 1939.

5. (*a*) Rubner, M.: Die Gesetze des Energieverbrauch bei der Ernährung, Leipzig, Franz Deuticke, 1902. (*b*) Lusk, G.: Animal Calorimetry: An Investigation into the Causes of the Specific Dynamic Action of the Foodstuffs, J. Biol. Chem. **20**:555, 1915.

6. Plaut, R.: Gaswechseluntersuchungen bei Fettsucht und Hypophysiserkrankungen, Deutsches Arch. f. klin. Med. **139**:285, 1922.

to observe an interrelation between specific dynamic action and the activity of the pituitary gland.[7]

No agreement exists among investigators in regard to the behavior of the specific dynamic action in obesity. A lower response than in normal persons is certainly not a consistent finding; many authorities have not observed it. In childhood and during puberty the interpretation is further complicated by the circumstance that during these periods of rapid growth the rise in heat production after food intake is generally lower than in adults.[8]

In my own observations made on 4 normal and 6 obese children, 9 to 13 years of age, no significant differences were noted. This part of the study was soon discontinued, since the preliminary examinations and the evidence from the literature made it unlikely that any new insight could be gained from further work in this direction.

In connection with the present paper, it is of interest to consider whether a portion of the possible conservation of energy in obesity may be the result of a depressed specific dynamic action. Plaut [6] and others have claimed that the deficit in heat production could account for the progressive accumulation of fat deposits. This argument is as debatable and unconvincing as the diagnosis of pituitary disorder on the basis of alleged changes in the specific dynamic action. The high specific dynamic response to food intake under normal conditions accounts for not more than 3 to 5 per cent of the total daily requirements for metabolism. Even if a low specific dynamic action were a true and regular finding, the saving in energy expenditure would be inadequate as an explanation of obesity. Furthermore, the food intake of obese patients is much larger than that of nonobese persons.[9] Any possible conservation in energy expenditure under experimental conditions in response to a small amount of protein would be overcompensated for by the cumulative effect of the excessive consumption of food throughout the day.

Summarizing the information on energy requirements for basal metabolism, for growth and for specific dynamic action, one must conclude that no significant difference exists between obese and normally nourished persons in these physiologic routes of expenditure of energy.

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7. (*a*) Johnston, M. W.: The Specific Dynamic Response to Protein of Individuals Suffering from Disease of the Hypophysis, J. Clin. Investigation **11**: 437, 1932. (*b*) Fulton, M. N., and Cushing, H.: The Specific Dynamic Action of Protein in Patients with Pituitary Disease, Arch. Int. Med. **50**:649 (Nov.) 1932.

8. Hilsinger, W.: Die spezifisch-dynamische Eiweisswirkung bei Kindern: II. Physiologische Werte, Arch. f. Kinderh. **81**:36, 1927.

9. (*a*) Kisch, F.: Ueber die Esssucht Schweradipöser, Ztschr. f. klin. Med. **132**:504, 1937. (*b*) Bruch.[1]

MUSCULAR ACTIVITY IN OBESITY

REVIEW OF THE LITERATURE

The great variation in the energy requirements of different persons results chiefly from differences in their muscular activity. In relation to obesity and possible conservation of energy, two questions arise: first, whether the transformation of energy for equal amounts of work is the same in normal and obese persons and, second, whether obese persons are active to the same extent as normal persons.

Both these possibilities, either separately or in combination, have been examined for their importance in the development of obesity. Early workers,[10] studying the energy consumption during muscular exercise, failed to observe differences between normal and obese persons. The comprehensive examinations of Lauter [11] led also to the conclusion that an obese person responds to exercise with an oxygen consumption the same as or higher than the normal person and that this can also be recognized during the period following exercise. In contrast to these observations, Bernhardt [12] made the startling claim that though it was true that the energy requirement of the obese person was normal during exercise, a distinct negative phase could be observed during the period following exercise, that in this after-phase the oxygen consumption might drop even below that necessary for basal metabolism and that this negative phase might compensate for the increased consumption during activity. Other workers who checked on Bernhardt's observations did not confirm his findings. Wilder and co-workers [13] stated that the heat production following exercise did not drop below the basal level at any time during two hours after exercise. Kommerell [14] demonstrated that the obese person, in addition to having a normal energy consumption during and after physical work, required considerably more energy for simple movements, since the larger mass of his body which had to be moved called for greater exertion.

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10. (*a*) Jaquet, A., and Svenson, N.: Zur Kenntnis des Stoffwechsels fettsüchtiger Individuen, Ztschr. f. klin. Med. **41**:375, 1900. (*b*) Broden, A., and Wolpert, H.: Respiratiorische Arbeitsversuche bei wechselnder Luftfeuchtigkeit an einer fetten Versuchsperson, Arch. f. Hyg. **39**:298, 1901.

11. Lauter, S.: Zur Genese der Fettsucht, Deutsches Arch. f. klin. Med. **150**: 315, 1926.

12. Bernhardt, H.: Zum Problem der Fettleibigkeit (Zugleich ein Beitrag zur Frage des sogenannten "Grundumsatzes"), Ergebn. d. inn. Med. u. Kinderh. **36**:1, 1929.

13. Wilder, R. M.; Smith, F. H., and Sandiford, I.: Observations on Obesity, Ann. Int. Med. **6**:724, 1932.

14. Kommerell, B.: Ueber den Arbeitsstoffwechsel bei der Fettsucht, Ztschr. f. klin. Med. **118**:474, 1931.

Thus there is no evidence that the obese person economizes through a different mechanism in transformation of energy during muscular activity. If conservation of energy plays a role in the production of obesity, it can be only as the result of diminished muscular exercise. This aspect of the energy problem is frequently mentioned in the clinical literature. According to von Noorden,[15] inactivity is one of the "exogenous" factors which may cause obesity, either alone or in combination with increased intake of food. Von Noorden's classification dominated the concepts concerning the pathogenesis of obesity for several decades, and reference to "inactivity" is found in nearly all publications dealing with adiposity. As evidence of the role of inactivity in the development of obesity, the authors usually cite the greater incidence of obesity with increased age and with sedentary habits of life, the differences in the occurrence of obesity in various occupational groups and the observation that most obese persons dislike strenuous exercise. The importance attributed to muscular inactivity in the pathogenesis of obesity varies greatly with the authors' theoretic concepts concerning the nature of obesity. Lauter,[11] whose extensive investigations of the metabolic processes in the obese had failed to demonstrate any physiologic abnormalities, emphasized the importance of energy economy through decreased muscular activity. He specifically stressed the considerable savings which might be effected through decrease in the small, everyday movements; their absence might account for the phlegmatic appearance of many obese persons. He correlated this inactivity to lack of psychic impulses but recorded no detailed observations concerning these factors.

Other authors considered differences in the activity of their patients as unimportant or of only secondary importance. Silver and Bauer,[16] emphasizing the constitutional factors, found no correlation between obesity and occupation. Gurney [17] compared a group of 75 stout women with a comparable group of nonstout women who had undergone approximately the same number of pregnancies and operations; he concluded that heredity and not environmental influences were of decisive importance in the development of obesity. In contrast, Greene,[18] in a recent contribution, found that diminished activity, mostly during illness and convalescence, was the most frequent factor in the causation of 350 cases of obesity.

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15. von Noorden, C.: Obesity, Metabolism and Practical Medicine, Chicago, V. T. Keener and Co., 1907, vol. 3, p. 693.

16. Silver, S., and Bauer, J.: Obesity, Constitutional or Endocrine? Am. J. M. Sc. **181**:769, 1931.

17. Gurney, R.: The Hereditary Factor in Obesity, Arch. Int. Med. **57**: 557 (March) 1936.

18. Greene, J. A.: Clinical Study of the Etiology of Obesity, Ann. Int. Med. **12**:1797, 1939.

Lurie [19] and Levy [20] described personality traits and behavior of obese children and adolescents whom they called patients with "pituitary disturbances" and "Fröhlich's syndrome." They both called attention to the lack of aggressiveness and to the slow, phlegmatic and submissive behavior of these patients. Lurie considered their pattern of reaction and their personality traits to be due to "hormonal deficiency." Levy concluded that the submissive behavior in these patients was due to a constitutional factor. He specifically emphasized that it could not be explained by the early life history, by a psychologic response to the obesity, by hypogenitalism or by the maternal attitude. Though the manifest behavior at the time of observation is described, the relation of activity to the development of obesity cannot be determined from these reports.

In my search through the extensive clinical and experimental literature on obesity, I have not succeeded in finding material which gave detailed information on the factor of muscular activity in relation to obesity. Only inconsistent and contradictory information is recorded concerning the frequency with which inactivity is observed in obese patients and concerning its relation to the onset of obesity and its significance in the personal development of the patients. This paper represents an attempt to describe and evaluate these different aspects of the problem.

PERSONAL OBSERVATIONS

Description of Subjects.—This report is based on observations made on 160 obese children (74 boys and 86 girls). Some children have been under observation for more than three years; others were seen for the first time only a few weeks ago. The study presents a cross sectional picture of the activities of these children. The development of individual patients who were studied more closely and observed over a longer period will be reported at a later date.

Information as to the degree of obesity (expressed as percentage of overweight by comparison of actual weight with data in the height-age-weight tables of Baldwin and Wood [21]), the age of the patient, his position in the family and the racial background has been summarized in table 1. The mixed population of the city of New York reflects itself in the multiple racial and national backgrounds of the patients in this study. All of the children were American-born, but most of their parents were foreign-born.

19. Lurie, L. A.: Endocrinology and the Understanding and Treatment of the Exceptional Child, J. A. M. A. **110**:1531 (May 7) 1938.

20. Levy, D. M.: Aggressive-Submissive Behavior and the Fröhlich Syndrome, Arch. Neurol. & Psychiat. **36**:991 (Nov.) 1936.

21. Baldwin, B. T., and Wood, T. D.: Weight-Height-Age Tables, New York, American Child Health Association, 1920.

The size of the families and the position of the patient in relation to siblings revealed striking features. The average size of the families was less than 2 children per family. The age difference between siblings was frequently large, from 5 to 10 years or more, the obese child being generally separated by a lapse of many years from the next older or younger child. The children who were the youngest or the only children in their families, hence permanently in the position of the "baby," represent 70 per cent of the total.

Collection and Evaluation of Information.—The information on physical activity of obese children was given by the parents and children,

TABLE 1.—*Data for One Hundred and Sixty Obese Children*

	74 Boys		86 Girls		160 Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Degree of Obesity Expressed as Percentage of Overweight *						
Moderate: 25 to 40	35	47.5	31	36	66	41
Severe: 40 to 70	33	44.5	43	50	76	48
Extreme: 70 to 120	6	8	12	14	18	11
Age in Years						
2 to 6	12	16	17	20	29	18
6 to 12	50	68	64	74	114	71
12 to 14	12	16	5	6	17	11
Family Position in Relation to Other Siblings						
Oldest	18	24	14	16	32	20
Between	7	10	8	10	15	10
Youngest	25	34	32	37	57	35
Only	24	32	32	37	56	35
Racial Background						
Jewish	42	57	42	49	84	52.5
North European	19	26	20	23	39	24
South European	8	11	9	11	17	11
American Negro	3	3	13	15	16	10
Mixed	2	3	2	2	4	2.5

* In comparison with the standards of Baldwin and Wood.[21]

either spontaneously or on questioning. In a number of cases additional information was obtained from the school authorities or by visits to the home.[22] Direct observations were made at the time of visits to the clinic. It was noted with great frequency that even older children (10 years or more) were unable to dress and undress themselves and accepted help from their parents in a matter-of-fact way, as if they were accustomed to being waited on. A similar attitude was sometimes expressed as soon as the patient and his mother entered the examination room. The room is equipped with one chair beside the desk of the physician, which is usually taken by the mother. Obese children often took the chair while the mother stood and remained seated, with the mother's approval, even when it was suggested that the chair be offered to the mother.

22. Mrs. Grace Touraine assisted in collecting the information.

From these observations the impression was gained that these were children accustomed to receive more deference and direct assistance in everyday tasks than is usual for children of comparable age. The inquiry into the daily activities was aimed at information concerning the degree of self care and independence, participation in household duties, behavior at school, ability to associate with other children and to partake in group activities and spontaneous interests and hobbies. In a number of cases observations on the type of movements, complaints referable to muscular exercise, the attitude of the patients and parents toward exercise and therapeutic suggestions were also recorded. The case histories have been collected over a period of several years, and not all of them contain complete material on these different aspects. As recurring problems became familiar, the inquiry became more detailed and specific. Some patients discontinued attendance at the clinic before detailed information could be obtained.

In evaluating the accumulated material for this report, only the information which referred to some specific aspect of the child's activity was included. Such general remarks as "normal" or "quite active" or "just lazy" were discarded, since they reflect only the subjective judgment of the person giving the information. It was frequently observed that children who were described as normal ("he gets along very well with everybody") were quiet and withdrawn and in reality had no one with whom to "get along."

The information on muscular activity obtained in this way cannot be expressed in caloric equivalents of energy expenditure. The case of a child who was rated as inactive will serve as an illustration that these detailed histories supply a fairly adequate picture of the type and extent of exercise, even though the information cannot be evaluated in exact figures.

Report of Case.—David B. was 9 years 9 months old when first seen. He was 60 per cent overweight. The gain in weight had become conspicuous after a tonsillectomy, which was performed when the patient was 3 years old. The parents were not concerned about his obesity, nor did they feel that his behavior and the degree of his activities were unusual. He was brought to the clinic only after repeated urging on the part of the school authorities.

Self Care: The child had made no attempt to dress himself until he was more than 8 years old; even at the time of examination he was so slow that his mother usually helped him. In the clinic he accepted dressing and undressing by his mother with such passiveness that he resembled a wooden mannequin. His mother continued to give him his baths. The boy had recently become increasingly modest and had asked to take his bath alone. The mother was afraid he might fall, since he was so heavy, and he became so frightened of this possibility that he was willing to wait "a few more years" before being allowed to bathe alone. The patient had been sick with otitis media as an infant, and walking was somewhat delayed (19 months). He started to talk early, and there was no delay in the eruption of teeth. Training in the control of bowels and bladder had been instituted early.

The boy, however, continued to wet himself during the night unless the mother picked him up several times. He did not take part in any way in the daily duties of the household. It had never occurred to his mother that she might send David to the store or let him do any small job around the house. Eating was the only thing which he did rapidly and without help and urging.

School: He first entered school when 6 years old. He liked it from the beginning and was quite advanced in reading. Otherwise he was slow and the school authorities drew the attention of the parents to his immature behavior and his lack of manual skill, which was so marked that he could not do such simple things for himself as hanging up his coat, using scissors or opening a closet door. His mother continued to take him to the school although he had to cross only one street, which was regulated by traffic lights.

Social Contact: He had never played with other children. When he was younger he wanted to play, but his mother "reasoned" with him and he stayed indoors and played by himself. Later he did not want to play with other children. He was afraid he might have to fight, and he did not know how to defend himself. He never entered into any games or athletic activities. When asked whether he liked to run he was somewhat astonished and answered: "I have nothing to run for."

Individual Activities: He liked best to read and to draw pictures, and he listened to music on the radio. He was taken to the movies about once a week. He played by himself and continued to be content with blocks, boxes and other toys generally used by younger children. He was always quiet and neat and never rough in his play.

Type of Movement: All movements were slow and awkward, and the boy stumbled quite often when walking. No neurologic abnormality was found on physical examination.

Attitude of Parents Toward Activity of Child: The patient was the first surviving child, and the parents were always much concerned about his health. When he was 3 years old tonsillectomy was performed as a preventive measure. Hemorrhage occurred after the operation. During the following two years occasional bleeding from the throat or nose occurred. His mother became even more careful with him and prevented him from playing actively. When he was not being kept indoors she took him for a quiet walk in the park. He was not sent to kindergarten because his parents feared he might have another hemorrhage.

Though the family lived in a good neighborhood, the mother did not approve of it and did not want her children to associate with other children. She was afraid to expose her boy to physical injury and to the moral dangers of the street. Once the patient came home and used "bad language" toward his younger sister. Only after much urging did the mother repeat the bad word he had used; the sister had interfered with his play and he had told her to "scram."

Cooperation of Parents: It was recommended that the patient should be encouraged to greater independence in his self care and should be given some duties in the household. In addition, supervised muscular exercise in the posture and massage clinic was advised. Since the mother had brought him to the clinic only after repeated urging by the school authorities and since she was satisfied with his behavior, her cooperation was poor and subsequent appointments were broken. The patient was seen only at the time of follow-up visits. His degree of inactivity had remained unchanged. The mother reported that it was not of much use to send him to the street or to the park for play. The other children teased him and would not allow him to join their games because he was so awkward.

Summary: Summarizing the activity of this patient, one is well entitled to call him an "inactive" child, and one is justified in assuming that he spends considerably less energy in muscular exercise than an average boy of his age. In addition to this quantitative aspect, there are other points of interest. The inability of this patient to take care of himself and the persistence of enuresis are indicative of delay in development of independence. This was present even before tonsillectomy at the age of 3. The operation and subsequent hemorrhages only strengthened this attitude and precipitated further protective measures, which prevented the patient from making normal social contacts with children of his age and from acquiring muscular skill. The inability to associate with children preceded the development of a severe degree of obesity. The teasing he suffers now about his condition seems to be a sequel and not the cause of his unsatisfactory social relationship.

Quantitative Information on Physical Activity.—The information about the different aspects of physical activity is not as complete in all cases as in the case described, nor is the interpretation of the degree of activity always as obvious. Some patients showed degrees of activity varying in the different aspects of behavior. An attempt was made to

TABLE 2.—*Classification of One Hundred and Forty Obese Children by Degree of Activity*

	66 Boys		74 Girls		140 Total	
Degree of Activity	Number	Percentage	Number	Percentage	Number	Percentage
Inactive	50	76	51	68	101	72
Mixed	4	6	7	9.5	11	8
Active	12	18	16	22.5	28	20

assess the degree of physical activity by one descriptive term. In view of the difficulties of doing so objectively, the following figures are given with some reserve; they serve merely to demonstrate general tendencies.

For 8 boys and 12 girls the information was inadequate, and the degree of activity could not be rated. Of the remaining 66 boys, 50 (76 per cent) were considered inactive. Twelve (18 per cent) gave a history of a normal degree of activity; in 4 (6 per cent) there was evidence of inactivity in some respects, simultaneously with normal activity in other regards. As for the 74 girls for whom adequate information was available, 51 (68 per cent) were rated as inactive, 16 (22.5 per cent) were normally active and 7 (9.5 per cent) gave a history of a combination of active and inactive behavior (table 2).

The case of a 3½ year old girl will serve as an example of such mixed degrees of activity. This child was moderately obese and liked to play with other children in the park, but she had wanted to be carried and had refused to walk since the birth of a baby brother six months before. The increase in weight had occurred during that period.

Another girl of 5 years played actively by herself, was fond of dancing and entered into supervised games, but she would not play with other children because she got into fights; so she had little active exercise and stayed indoors most of the time.

The impression was gained that the younger children were less frequently inactive than the children of school age (table 3). For 3 of the 12 boys under 6 years of age no information was available. Of the remaining 9 boys, 5 (55 per cent) were described as inactive and 4 (45 per cent) as active. The differences were more marked in girls. Of 17 girls under 6 years of age, adequate information had been obtained for 11. Of these, only 2 (18.5 per cent) were rated inactive; both these girls were more than 5 years of age. In 5 girls (45 per cent) the degree of activity was considered normal; in 4 instances (36.5 per cent) a mixture of physical activity and inactivity was recorded. These children are included in the figures given in table 2 for the whole group.

TABLE 3.—*Classification of Twenty Young Obese Children by Degree of Activity*

	9 Boys Under 6 Years		11 Girls Under 6 Years		20 Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Degree of Activity						
Inactive	5	55	2	18.5	7	35
Mixed	..	..	4	36.5	4	20
Active	4	45	5	45	9	45

TABLE 4.—*Classification by Degree of Obesity of One Hundred and One Inactive Subjects in a Group of One Hundred and Sixty Obese Children*

	101 Inactive Children						Entire Group of 160 Obese Children	
	50 Boys		51 Girls		101 Total			
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Degree of Obesity Expressed as Percentage of Overweight *								
Moderate: 25 to 40	21	42	16	31	37	36.6	66	41
Severe: 40 to 70	23	46	28	55	51	50.5	76	48
Extreme: 70 to 120	6	12	7	14	13	12.9	18	11

* In comparison with the standards of Baldwin and Wood.[21]

Since the number of children in the younger age group is small, this finding awaits confirmation through further observation. That changes in the degree of activity occur was corroborated by the not infrequent history that older children who were markedly inactive at the time of examination had been active and aggressive children when younger. Another change in the degree of activity seems to occur after puberty; a number of patients who were followed for several years and who were inactive and withdrawn when first seen displayed more active interests during adolescence.

No relation was found between the rating for activity and the severity of the weight excess. The distribution according to degree of obesity of the 50 inactive boys resembled that of the total group; 21 (42 per cent) were moderately obese; in 23 (46 per cent) the condition was

severe and in 6 (12 per cent) extreme. The percentile figures for the total number of boys were 47.5, 44.5 and 8 respectively. The distribution for the 51 inactive girls was as follows: 16 (31 per cent) moderate, 28 (55 per cent) severe and 7 (14 per cent) extreme. The figures for the total number of girls were 36 per cent, 50 per cent and 14 per cent respectively (table 4).

Self Care and Participation in Family Life.—Inquiry into this aspect of daily routine had been stimulated by the direct observation at the time of visits to the clinic that many obese children were extremely dependent on assistance even for simple tasks of everyday life. Information was obtained relating to the patients' ability to perform such tasks as dressing, feeding and bathing themselves and their interest and willingness to participate in the household chores.

The evaluation of these two factors is influenced by the age of the child. A child of 6 years may or may not be able to tie his shoe laces. If one of 10 or 12 years is unable to do so, it strongly suggests prolongation of infantile dependence; and a boy of 14 years whose mother goes down on her knees to put socks on his feet certainly exhibits abnormal delay in self care. In rating the information, allowance was made for a wide range in the ages at which the different performances should be acquired; even if the expectancy was placed fairly high, the frequency with which obese children were unable to take care of themselves was great.

Adequate information was obtained for 100 children (46 boys and 54 girls). Only 23 of these children had acquired a degree of independent self care which was in harmony with their ages. The majority (77) exhibited a striking delay in their ability, as well as in their willingness, to take care of themselves.

The question arises whether the locomotor development had been retarded and whether the observed delay in acquiring the usual skills was the expression of a physical defect. It has been reported previously that this type of obese patient showed no signs of physical or mental retardation in early development.[4] The previous statement was based on information obtained for 40 children. Reevaluation of this factor in this larger group corroborated the earlier observation. Information on locomotor development was obtained for 144 children. Onset of walking was normal or even early in 134 of them. Ten children had not started to walk before 18 months; in no case was there a delay beyond 26 months. Of these 10 children, 3 had suffered from rickets during infancy, 2 had congenital deformities of the feet and 1 showed signs of dyschondroplasia.

These figures make it unlikely that an innate physical disability was responsible for the retardation in independent behavior. Rather, it

seems to have been due to a defect in training and to a delay in assuming normal responsibilities. At the same time it reveals a distrust on the part of the mothers in the capacities of their children. This feeling was frequently expressed in the comments made. "I think I do it neater and quicker" was a frequent explanation of why a mother would not allow her growing child to dress himself. A desire to do things for themselves generally existed in the young children, but after the age of 5 or 6 years they gradually lost all interest in becoming independent. If demands were made on them later, they were so slow and awkward that they became easily discouraged, especially when the mothers were irritated by their slowness and impatiently nagged and continued to help them.

The lack of independence sometimes extended to every detail of daily life; there were children 10 years of age and more who had not had a single bowel movement without being coaxed to go to the bathroom. Some children of more than 6 and 8 years were still spoon fed.

Another expression of persistence at an immature level of responsibility was the frequency with which bed wetting occurred. The information concerning training in urinary control is incomplete; it was not recorded in 85 instances. In 33 of 75 patients about whom an inquiry was made enuresis was present, an incidence of 44 per cent. The same incidence was observed among 40 other patients who were studied more closely and in all of whom the presence or absence of enuresis had been investigated. Its presence was admitted in 16 patients (40 per cent). Five of these 16 patients were more than 10 years of age, and only 1 was under 6 years of age. Enuresis was a more severe and more frequent symptom in obese boys.

Even more conspicuous than the inability to care for themselves was the lack of interest and willingness to take part in the ordinary household duties frequently performed by children. Questions concerning this point were answered by the mother with a certain degree of amazement, especially if the children were young. But hostile and derogatory remarks about "selfishness" and "laziness" were not infrequent if the question referred to an older child. Apparently the idea of expecting some assistance from their children did not occur to many of these mothers until the children approached the age of puberty, and then they were disappointed by the inability and refusal of the children.

In a few instances the demands made on the children to assist in household chores were excessive, even to the extent of interfering with outside contacts and with outdoor games. Such instances were rare—only 3 or 4 in the whole group. As a rule, the children who were helplessly dependent and who had no household obligations made little or no social contacts and avoided active games and exercise.

How important a factor this lack of independent self care constitutes in the energy balance and the development of obesity cannot be exactly estimated. Even if the caloric equivalent for the single performances is not high, they may account in their cumulative effect for a considerable conservation in energy expenditure. More important seems to be their role in the formation of habits and their psychologic implications. The children develop a passive attitude toward life; they learn to expect that everything will be done for them. They fail to acquire skill and experience in the more complex muscular activities, and they do not know the pleasure and satisfaction of independent achievements.

School Life.—Most of the children in this study were of school age. A few of the younger children attended kindergarten or nursery school; this, however, only after it had been recommended to the parents. Few children had been sent spontaneously to kindergarten.

For many of these children school represented the first opportunity for contact with other children. The adjustment to this new situation varied a good deal, and it represented a real problem for many.

The importance of the school for the physical activities of children lies on the one hand in the actual opportunities for exercise provided by the school and on the other hand in its interference with outdoor play and exercise by the demands it makes on a large portion of the children's time. In the lower grades opportunity for play is given during recess. Whether a child spends this period as an active partner or a passive onlooker at games depends largely on his relation to other children. As judged by the information obtained, obese children seldom entered into the games of other children. In the higher grades, regular periods for gymnastic exercises are provided in most schools. Only a few of the obese children enjoyed this opportunity for supervised exercise and organized games; the majority tried to avoid it and used every conceivable excuse to absent themselves from the gymnastic period. They frequently made the request for a medical certificate that their physical condition did not permit them to enter into active games or to take part in athletics. The information concerning this aspect was not obtained regularly; therefore, no figures are given. But the impression was gained that obese children generally make little use of the opportunities for muscular exercise provided by the school.

The time spent in school rooms and over school assignments is, of course, not available for active exercise. The majority of the obese children were good students. They were not only of good or superior intelligence but also ambitious to pass with high marks. Generally the questions concerning school achievement were answered with much more enthusiasm than the inquiry into other aspects of their lives. Information about successes in school work was frequently given instead of an answer to some question relating to achievements in physical exercise.

The working habits of most children were definitely slow, and probably more time was spent on school assignments than the average child devotes to them. In addition, many children attended a second school for national or religious training. The schedules of many children were so crowded, especially of older children who had to go some distance to high school, that there was little or no time left for any other activity.

This factor, however, was of only secondary importance. During the long periods of vacation the fundamentally passive child remained inactive and gained even more weight than during periods of school attendance. Many mothers stated that they continued to send a child to the afternoon classes "to keep him out of the kitchen" or because "he would not go down to play and would eat all the time." A smaller group of children for whom the long school hours represented a mechanical interference with the carrying out of a desire for activity took advantage of the greater opportunity for exercise and generally lost weight during summer vacations.

It was noted frequently that the parents were unwilling to give up protective custody over their children after they had entered school. They continued to accompany them to and from school, even at an advanced age when children can normally be trusted to take care of themselves in traffic. Some mothers had taken apartments near the school, preferably in the same block, sometimes without any consideration for the convenience of the husbands. If they finally consented to let their children walk to school unaccompanied, they would spend tense and anxious minutes at the window watching every step between home and school and carefully checking off every second. In reporting these facts many mothers complained about the "lack of understanding" on the part of the teacher. The mother of an 8 year old girl was bitter against the new teacher who did not permit her to come upstairs and accompany her child to the classroom door in order to help her take off her coat and hat.

The same mistrust in the child's ability to take care of his own affairs expressed itself in the frequency with which the mothers dashed to the school to complain of some injustice done to their children either by the teacher or by the schoolmates. The mother of an 11 year old boy reported with great resentment the remark of the principal when she came with another complaint: "Well, is mother back with the baby again?"—a truly fitting description of the situation.

Active Games and Social Contacts.—Active games of children, sports and athletics are so closely connected with comradeship and stimulating competition that it is not feasible to discuss one without the other. Questions concerning the extent of outdoor and group activities were frequently answered by reference to friends and playmates. These two aspects of a child's activity, however, do not always coincide. The

pertinent figures are presented in table 5. For 25 children no information was recorded. Of the remaining 135 children, 68 (50 per cent) had no friends or playmates and did not carry out any exercise by themselves.

The terms "friends" and "no friends" are used in this evaluation to indicate the presence or absence of suitable playmates. Some of the older children who are classified as having no friends were "perfectly happy to have a bunch of little children around them" or "loved to kiss little babies" or were boys who played with younger girls only. The majority, however, of the children who are listed as having no friends had no one to play with and kept very much to themselves. The information was given with monotonous repetition: "The other children are too rough." "There are no nice children in our neighborhood." "The other children call her fat stuff; then she runs home and cries." "I wanted to give him a birthday party, but he had no friends to invite." In the case of an 8 year old boy the mother complained: "Even the girls chase him away."

TABLE 5.—*Classification of One Hundred and Sixty Obese Children on the Basis of Social Adjustment*

	Degree of Activity of Children									
	32 Active			92 Nonactive			36 No Information			
Social Adjustment	Boys	Girls	Total	Boys	Girls	Total	Boys	Girls	Total	Total
Friends.....	11	12	23	8	13	21	2	..	2	46
No friends.....	6	1	7	32	36	68	4	5	9	84
No information.....	..	2	2	3	..	3	8	17	25	30

Some children associated only with other children "of the same temperament" or had as playmate for "nice, quiet games" some sick, crippled or otherwise defective child. They are listed as nonactive children having friends. Twenty-one children fall into this group.

The children were not always willing to admit this lack of companionship or their unpopularity. They claimed that they played "with the whole block" or "they all are my friends," while unable to name one single child as a personal friend. Others freely expressed their dislike or fear of other children or joined their mothers in complaints about the "bad" children in that particular neighborhood, who were rough and wild and called their fat neighbors "sissy."

The terms "active" and "nonactive" are used in this connection to describe the participation in or avoidance of active games and sports, such as running games, skating, swimming, ball games, hiking and bicycle riding. It is, of course, difficult to determine what the information concerning all these activities means. A boy who is said to "love football" may satisfy his fondness for that game by listening with excitement to the report over the radio. Even those who take part in such games are

not necessarily active physically. One boy of 12, who is listed as sociable and active, had a wide range of interests; he is probably the most alert boy in the whole group. His mother, speaking about his activities, mentioned that his nickname was "the politician." "He lets the other fellow do the work. If he goes down to play baseball, he keeps score; and if he works on the newspaper, he takes the part of the editor and lets the others run about as reporters." If patients with this kind of restriction of activity had been considered "nonactive," a very small number, and young children only, could have been listed as active. The term "nonactive" indicates a definite disinclination, refusal or even fear on the part of the child to enter into any active games or to learn something that requires muscular exertion and skill. A few children liked to swim, roller skate or hike by themselves; they are listed as active but having no friends.

Information concerning participation in active games was recorded for 124 children; 92 (74 per cent) did not enter into the games of their contemporaries and preferred sedentary occupations. A marked fear of falling and of other dangers of sports and activities was frequently expressed by the children.

The number of inactive children was greater than the number without friends; of 120 children about whom information was obtained, 40 (35 per cent) mingled freely with other children or had at least a few congenial friends; 84 (65 per cent) were seclusive and withdrawn and encountered marked difficulty in their occasional attempts to associate with other children.

The question arises as to how far these social difficulties are the result of the obesity. Many of the children complained of being heckled and teased about their condition, and it was felt in the beginning of this study that the unsatisfactory social relations had developed as a reaction to these repeated psychologic traumas. Investigation of the past history revealed such a connection in only a few exceptional cases.

One girl of 13 years, who was tremendously stout, is an example of these unusual patients. She had grown up in a small community in Pennsylvania. Though she was much overweight, nobody paid particular attention to her obesity, and she experienced no difficulty in mixing with other children. When she was 9 years old the family moved to New York. She was greatly embarrassed about being stared at and felt hurt by derisive remarks about her experience.

In the great majority of the patients, the tendency to keep apart and to avoid vigorous activity could be traced to a time before any severe degree of obesity had developed. However, only a few children were described as having been "always quiet." The majority had been active in the preschool age, and most of the young children, though much over-

weight, had no inhibition in playing with other children. Some of the small children were aggressive toward other children, and this very aggressiveness tended to make them undesirable playmates. This tendency still showed itself in some older children who, in a cowardly way, avoided competition and fights with children of their own age but bullied children smaller and weaker than themselves. In other instances some definite event in the life of the child was associated with a change in his activities. This problem will be discussed later in relation to the onset of obesity.

Recreational Activities Other Than Exercise.—In view of the fact that so many obese children had no friends and did not participate in active games, it was of interest to learn what constituted their recreational activities. Reference has already been made to the long hours spent by some of the children in schools and on school assignments. Reviewing the information obtained for 96 patients, one is struck by the paucity of interests and talents revealed in this group of intelligent children. In many cases even persistent questioning did not produce information beyond "just likes to take it easy," "would stay in bed all day," "nothing interests her," "food is all she thinks of" and "just sits about."

Radio and movies played a paramount role as occupations for spare time. For 40 of the 96 children it was specifically emphasized that these two were the favorite entertainment. "He would go to the movies every day and talks about it all the time." A few children managed to go five to six times a week; three to four times was not unusual, and "sits through each performance twice" and "spends all Saturday at the movies" or "there on all rainy days to keep him off the street" were frequent descriptions.

Many children listened with the same persistence and monotony to one radio performance after another. "From 5 o'clock on he won't move; he just sits indoors all the time and has the radio going; he won't move from his chair, not even for eating" was the description from the mother of a 12 year old boy, and it well fitted the information obtained for many other children. This desire for passive entertainment was in many instances coupled with a demand for food. It was reported frequently that the children nibbled sweets or ate bread while listening to the radio. One girl of 11 stated: "I don't feel like having been to the movies if I don't have my bar of candy."

Next to movies and radio, reading was most frequently mentioned as a pastime. In view of the good intellectual development of many of these obese children, it is astonishing how many were satisfied with the comic strip level of reading. A smaller number were voracious readers of more serious literature, preferring geography, history and adventure stories. No figures are given on this aspect, since the information is probably incomplete.

For only 20 children were more individual spontaneous interests recorded. In 3 instances, with a boy in 1 case, cooking was a chief interest. Some others displayed skill and creative ability in arts, especially drawing, or in crafts like needlework and weaving, carpentry, aeroplane construction and other technical works. One girl of 11 liked to write poems; a few were interested in music and singing. The majority of the children, however, displayed little indication of creative self expression.

Type of Movements.—The most common characteristic of the bodily movements of many obese children was the slowness with which they were performed. In some instances this was also noticed in their speech and mimic. Some children showed so little change in their facial expressions that they resembled postencephalitic patients with a "mask face"; in no instance, however, did the past history contain a reference to encephalitis.

Poor coordination and clumsiness were frequently noted, sometimes extending to speech and gait. No neurologic disturbances, however, were observed.

Varying degrees of involuntary restlessness, twitching and tics were noted in 33 patients. In 42 instances no information concerning this point was recorded. Other children were described as sluggish, slow and showing low muscular tonus and poor posture. Many of the inactive children were talkative. The figures are not complete enough to warrant a statement concerning the frequency of these different observations. In some instances an aimless restlessness stood in marked contrast to the absence of voluntary exercise. Some parents who were good observers remarked: "He is restless all the time and yet quite inactive."

From the point of view of muscular physiology these two types of muscular movement have to be considered as different from each other.[23] This problem and its significance in obesity of childhood is in need of further study.

Contrary to the statements found in reports on adiposity in adults, complaints of discomfort referable to the burden of weight are conspicuous by their rarity in obese children. One patient suffered from cyanosis and dyspnea on slight exertion. Fear about sexual maldevelopment was marked in this patient. The dyspnea disappeared as soon as he had been reassured concerning his development and before he had lost any weight. A few other patients became short winded on strenuous exercise or when climbing several flights of stairs. No significant circulatory disturbances which interfered with ordinary

23. Bainbridge, F. A.: The Physiology of Muscular Exercise, rewritten by A. U. Bach and D. B. Dill, ed. 3, London, Longmans, Green & Co., 1931.

muscular activity were noted in this group. The high blood pressure which is a frequent concomitant of obesity in childhood deserves a different explanation.

Complaints about fatigue were not uncommon, but they related more to lack of initiative and general listlessness than to the result of physical activity. Pains in the feet and various degrees of pes planus were noted, but rarely was the discomfort sufficient to induce the patient to cooperate in the plan of treatment. The most frequent complaint was "excessive" perspiration. This complaint was made in most instances during the hot summer months. Only in a few instances was the observed degree of perspiration abnormally high. In the majority of cases actual observation did not bear out the description "excessive."

Two children suffered from skeletal disorders (dyschondroplasia with coxa vara and spondylolisthesis); in both the pathologic changes preceded the development of a marked degree of obesity.

Children who had no inhibition in their social relations and who participated in active sports did not complain of discomfort referable to the weight excess, though they sometimes did not attain the speed and skill developed by their slim companions.

Attitude of Parents and Onset of Obesity.—It was of interest to learn what role the parents and their attitudes toward physical exercise and social contacts had played in inhibiting their children from developing normal muscular capacities. Information on this point was obtained in 116 cases; in 44 cases nothing relating to this aspect was recorded. The parents expressed their attitudes freely and were frequently unwilling to change them. Most parents expressed complex opinions, sometimes contradictory and ambivalent. The following figures represent the one aspect which was most obvious.

Only 20 parents (18 per cent) had encouraged their children to associate with other children and to develop their physical prowess. In this group 16 children were rated as active, 2 as showing a mixture of active and inactive traits and 2 as inactive; these last 2 patients were boys of 12 years who were quite absorbed in their studies.

In 74 cases (65 per cent) the parents, in most instances the mother, expressed marked concern and fears about the safety of their children if they were outdoors and outside their supervision. The expressions "I never let him . . ." or "I would not allow . . ." recurred over and over again in their statements. The parallelism of this apprehensive attitude of the parents and marked inactivity of the children is striking. Practically all these children were timid and inactive; a few still showed some interest in physical activities.

In 8 cases no definite attitude concerning the activity of the child was expressed, but the parents did not cooperate by following any advice that might result in a change of the state of inactivity. Seventeen

parents made only derisory and critical remarks about their children's inactivity and were irritated and annoyed by their clumsiness and slowness. Many other parents used derogatory expressions when describing their children's inactivity; they are counted in the previous group, since anxiety was the more conspicuous attitude. In investigating the developmental history of this inactivity, it was found that in all cases these same parents had not allowed their children to develop free expression of their abilities. As an example the case of a 12 year old boy will be cited.

His mother could scarcely be stopped in an untiring flow of complaints against him "He is a coward," "not a real boy," "he has no interests," "I could kill him," "we sacrificed everything for him" and "he cannot do this and he cannot do that." The patient was a clumsy, slow and unfriendly boy. He was an only child and had been led and overprotected all his life.

The parental overconcern had become even more confining after the patient had had otitis and mastoiditis when 6 years old. At the same time a "heart murmur" had been observed. For the next two years the boy was pushed about in a baby carriage. Later, he was not allowed to play in the park, because the mother had heard too often of "children being killed." The same association, that he might be killed, came to her mind when it was suggested that the boy should come alone to the clinic (he lived only a short distance away). He was, at 12 years, not allowed to walk off the block by himself. If he went to the street to play, the mother went too. He was ashamed to have her hovering around and would soon return to the apartment to listen to the radio. This patient had started to gain weight excessively after the age of 6.

As in this case, many parents justified the limitations they placed on their children by referring to physical disorders, in most instances exaggerated minor ailments. Frequently, several reasons were given or new complaints were produced as soon as fear concerning one point had been dispelled. The finding of a heart murmur had repeatedly caused far reaching measures to "prevent cardiac disease." In a few cases the patient had had an attack of rheumatic fever; even though the process had been inactive for several years, reassurance was of little avail to persuade the parents in such cases to allow their children more freedom. Fear of contagious diseases was a frequent reason why the children had not been sent to kindergarten and had "never" been allowed to play with other children before entering school. The mother of a 5 year old Italian girl reported proudly: "She never moved from me more than from here to there," indicating a distance of about 3 yards. The child was tremendously obese, 120 per cent overweight for height and age. Hospitalization was advised in view of the severity of the condition; this was refused by the parents, who feared that the child might contract some infection and die in the hospital. Fear of common cold was mentioned even more frequently as a reason why children were not allowed to take part in the active games of other children. "My

mother says don't run; you get perspired and catch cold" reported a 6 year old boy who wanted to be active and was anxious to mingle with other children.

The possibility of disease and physical injury represented only one series of "dangers." Fear of bad moral influences was just as potent a reason for confining the children to the home and to the company of the mother. Many mothers took great credit for the "innocence" of their growing children who had never used rough or bad words. "Poor neighborhood" was a frequent complaint, quite independent of the quality of the neighborhood. Some mothers felt hurt because other children made fun of their children, or they feared their boys were not able to compete with other children because they were so "feminine"; this fear generally became greatly aggravated after a diagnosis of "endocrine disorder" had been made.

TABLE 6.—*Data Concerning Onset of Obesity in One Hundred and Fifty-Two Children*

Onset of Obesity	Boys	Girls	Total
"Always obese"	14	23	37
"Gradual"	12	12	24
Before 6 years	7	11	18
After 6 years	14	18	32
After 10 years	4	..	4
After removal of tonsils and adenoids	8	5	13
After other operations	5	1	6
After pertussis	1	5	6
After or coinciding with other diseases	4	3	7
After death of relatives	2	3	5

The different reasons offered in explanation of the morbid type of upbringing of these patients are too various to be enumerated in detail. In all such cases, however, overprotective features in the handling could be traced back to periods before the stated reason had been present and before marked obesity had developed. In many cases the fact that a child was "the only one" or "the baby, you know" was considered sufficient justification for keeping him from all social contacts and from normal activities.

The influence of this parental attitude, which projected death and danger into all movements of the child, was compared with the significance of the event to which the onset of the obesity was related. In 152 cases more or less reliable information was obtained; in 8 cases no information was recorded (table 6).

The rapid increase in weight was related to some definite event, such as an operation or disease of the patient or death or accident of a relative, in 37 cases (25 per cent). In a large number of cases, in which the parents remembered only the age at which the patient had grown obese, a review of the life history pointed to some experience coinciding with

the age of onset which might have been of a similar pathogenetic significance. Connection of this kind can be demonstrated only through detailed individual case histories; it is beyond the scope of the present paper to report a large series of case studies.

By way of an example the case of an 8 year old boy will be cited. He had become stout after the age of 3. It was difficult to believe that this timid and apprehensive fat boy had ever been a lively and active child. The mother told that "he was after the little fellow" when a brother was born, who is 3 years younger than the patient. She spoke of her way of handling the patient's aggressiveness as "I broke the heart in him." One may conclude that the child's change in behavior and the development of obesity stood in some connection to this experience, although the parents did not mention it in connection with the onset of obesity. Proof for this conclusion could be obtained only through an investigation of unconscious mental processes. The present report is based entirely on evaluation of conscious information, as remembered and reported by the patients or their parents.

Finally, I should like to point to the group of 32 children who gained excessively after 6 years of age, that is, following entrance into school. It is conceivable that for these children, who previously had lived in the company of adults only, contact with a group of active and inconsiderate children presented threatening problems that were beyond their capacity for adjustment.

Therapeutic Implications.—It is obvious that therapeutic suggestions should be given in accordance with individual difficulties and must take into account the different meaning and significance which social contacts and active games have for many obese children. Instead of being a source of satisfaction and pleasure, as they are for normal children, they are closely associated with the idea of danger and insecurity. It is of little value to tell such a fat child to join the others in their vigorous games. He has no chance of successful competition; ridicule and failure will only aggravate his fears and feeling of inferiority.

In many cases the first task will be to let the child perform that part of personal care which is compatible with his age and to give him some duty in the household and work to do for others, so that he may develop some understanding of active giving instead of passive receiving only.

For children with poor muscular development and postural defects a regular program of muscular training is indicated, but one must avoid letting these exercises become a dull and tedious task which serves only to increase the child's dislike for activities. If the patients are timid and helpless in their dealing with other children, it is advisable to give them opportunities for contact with other children such as are provided by supervised play groups, or clubs or scout organizations, which can

help them gradually develop better muscular skill and learn that there is "something to run for" in common games and contests.

Children, previously active, in whom inactivity has followed some recent experience have less difficulty in resuming social contacts. Such temporary states of inactivity may have been precipitated by a confining illness or may have been the reaction to some upsetting information, such as the fear of sexual maldevelopment constitutes for obese boys, for whom this diagnosis is frequently made erroneously. A pertinent case was reported in the paper on the food intake of obese children.[1]

The success of a therapeutic program for obese children depends largely on their ability and willingness to cooperate. By no means all patients or parents who were seen during this investigation were concerned about the obesity or inactivity; some plainly stated that they wished for no change. In others, attempts at changing the habits of eating or activity precipitated marked anxiety, which prevented constructive cooperation.

This investigation into the developmental history of obese children has attempted to arrive at an understanding of the underlying emotional disturbances. This insight is not only of theoretic interest but of practical value in the treatment of obese children, if therapy aims at more than temporary loss of weight and attempts also to help these children to become happier and better adjusted.

COMMENT

The considerations presented in this paper will be discussed in combination with the observations on food intake which were previously reported.[1] By limiting the discussion to these two aspects of the obesity problem, other aspects which probably are of equal importance are deliberately neglected.

The assumption that excessive body weight is the result of a disproportion between energy intake and output has been confirmed by the evaluation of the information obtained from a large group of obese children. In 80 per cent of the patients the food intake admittedly exceeded that of nonobese children; in the remaining 20 per cent analysis of the available information suggested that the food intake had been excessively high, at least during the period of rapid increase in weight. The amount of energy released through muscular exercise was found to be smaller than normal in more than 70 per cent of the patients. Thus in the majority of these obese children both factors, excessive intake of food and decreasing expenditure of energy, acted together in bringing about the progressive storage of fat.

This statement, however, merely describes a part of the mechanism by which the organism increases its weight and leaves unanswered the

question as to why the normal energy balance is disturbed. Under physiologic conditions the food intake parallels the energy expended in muscular work. This relation is disturbed in obese patients. In the previous paper a review of the known factors of weight regulation was presented. Clinical and experimental evidence pointed to the hypothalamus as the site of the physiologic disturbance in weight regulation. The importance of emotional experiences as a cause of alterations in hypothalamic regulation was emphasized.

The investigation of the emotional significance, for obese children, of food intake and muscular activity revealed that the emotional values of these two factors are opposed to each other. Food has an exaggerated value and stands for love, security and satisfaction; muscular activity is associated for many with the concept of danger, threat and insecurity. The associated occurrence of love of food and avoidance of muscular activity becomes comprehensible if considered from a psychologic point of view. Insecurity and delay in social and emotional maturation, which express themselves in the decreased muscular activity, appear to be the more fundamental disturbances; the excessive desire for food may be looked on as a compensatory mechanism which is called into play at times when the bodily integrity and the emotional security of the child are endangered. From the study of the personality and emotional development of these patients the impression was also gained that large body size is not only a mechanical sequel of a positive energy balance but has in itself an emotional significance for the child. Analysis of the observations from this point of view will be reported at a later date.

Inquiry into the life history of obese patients demonstrated that the associated muscular inactivity is a disturbance more complex than can be explained by hormonal imbalance or inherent incapacity alone. It is a manifestation of emotional life experiences which did not permit normal development of the muscular function. As with any other function, constant use is necessary to achieve the full development of muscular proficiency. Obviously, use does not create a new capacity, and it may be that the inherent drive for muscular exertion is originally not a strong trait in some obese children.

In the report on food intake attention was directed toward the family situation in which this particular attitude toward food had developed. A more detailed report on the family setting of obese children is in preparation; therefore, further discussion of this factor will be omitted in this paper.[24] It must be emphasized that even a specific environment does not in itself explain the occurrence of obesity in children reared

24. Bruch, H., and Touraine, G.: Obesity in Childhood: V. The Family Frame of Obese Children, Psychosom. Med. **2**:141 (April) 1940.

under these conditions. Disturbances in many different functions, on the somatic as well as on the emotional level, are necessary before obesity becomes manifest.

Life situations, as they were observed in this group of patients, tend to provoke increase in the desire for food and decrease in activity only in a certain type of person with certain definite characteristics. It is customary to call these innate qualities of a person his "constitution." The decisive influence which emotional forces have on the development of the symptoms essential for the pathogenesis of obesity militates against a concept of "constitution" identical with "inevitable destiny" [16] or of an otherwise mysterious factor which just "causes" certain behavior traits. To do justice to the complexity of the true clinical problem a wider, more dynamic concept of constitution is needed—a concept which identifies constitution not only with certain structural properties, such as manifest themselves in anatomic and physiologic changes, but which implies also certain dynamic qualities which express themselves in personality traits and emotional responsiveness. Draper,[25] in his work on the constitution underlying various diseases, emphasized these different aspects of constitution.

I should like to compare this dynamic concept to the phenomenon of resonance in acoustics, citing the familiar observation that a string may vibrate and produce a sound of a certain pitch when another string some distance away has been struck. Equality in the lengths of the two strings or some other simple proportional relation is a prerequisite for its occurrence. Some one unfamiliar with this phenomenon and wishing to study it might begin by determining all the measurable properties of the resting strings. He would not gain insight into the problem, however, until he learned about acoustic waves and found that the strings have also certain dynamic qualities, namely, the capacity to produce or to respond to acoustic waves of a definite frequency. The wave frequency, the pitch of the sound produced and the physical properties of the strings are interrelated functions.

In terms of the constitutional problem in obesity, the sound corresponds to the manifest symptoms, such as increased appetite or decreased activity, which record themselves by producing obesity. The measurable characteristics of the resting string may be likened to the structural aspects of constitution. The waves, which are as essential for producing the sound as are the properties of the string, represent the dynamic environment without which the symptom would not be released. This analogy illustrates why not all children living under apparently identical environmental conditions become obese. In order to have such an effect, the "environment" must be a function of the physical and dynamic

25. Draper, G.: Human Constitution: A Consideration of Its Relationship to Disease, Philadelphia, W. B. Saunders Company, 1924.

qualities of the organism. In other words, "environmental" factors, including the emotional milieu, are not entirely "outside" the individual. By contrasting "constitution" with "environment" an artificial and misleading dichotomy is implied, which is as little justified as is the term "exogenous" when used to designate the increased food intake and decreased activity of obese children.

SUMMARY

The different aspects of energy expenditure are discussed in relation to obesity. There is no valid evidence that the energy requirements for basal metabolism, for growth or for specific dynamic action are lower in the obese than in the normal child.

The mechanism of transformation of energy during muscular activity is not abnormal in the obese person.

An inquiry into various aspects of muscular activity of 160 obese children was made. Relevant information was obtained for 140.

Seventy-six per cent of the boys and 68 per cent of the girls were considered to be physically inactive. Eighteen per cent of the boys and 22.5 per cent of the girls showed a normal degree of activity. In 6 per cent of the boys and 9.5 per cent of the girls a combination of active and inactive traits was observed.

No relation was observed between severity of obesity and degree of activity. Younger children tended to be more active than children of school age. The impression was gained that another change, from inactive to more active behavior, occurred at adolescence.

Marked delay in ability and willingness to take care of themselves was observed in 77 per cent of obese children. A parallel expression of immaturity was the persistence of enuresis in more than 40 per cent of the children in whom this symptom was studied. Enuresis was more frequent and more severe in obese boys.

Entrance into school represented for many obese children the first opportunity for social contacts. Few obese children made use of the opportunities for muscular exercise provided by the school.

In 135 cases information on the frequency of social contacts and participation in active games was obtained. Fifty per cent of the children were both inactive and without playmates; 74 per cent did not take part in active games; 65 per cent had marked difficulties in social contacts.

The recreational activities, other than muscular exercise, showed little indication of creative self expression. In only 20 per cent were specific individual interests recorded. The majority of the children sought entertainment in frequenting movies, persistent listening to the radio and reading at the comic strip level.

The bodily movements of most obese children were slow. In a number of children varying degrees of involuntary restlessness, twitching and tics were noted. This restlessness was present in some patients characterized otherwise by marked inactivity. Complaints referable to the burden of weight were rare.

A striking parallelism was observed between marked apprehension of the parents concerning the dangers of social contact and physical exercise and inactivity of the children. Only a small number of parents had encouraged activities. This problem is discussed in relation to the time of onset of obesity.

A therapeutic program for the obese child should take account of the emotional significance of exercise, both for the patient and for the parents, and should not make demands which are beyond their capacity of cooperation.

A comparison of food intake and muscular activity revealed that these two factors have an opposed emotional value. On this basis the increased food intake of the obese child in the presence of decreased muscular activity becomes comprehensible.

Inquiry into the life histories of the patients revealed the importance of emotional influences in the development of inactivity. These emotional factors, however, become effective only in children with certain "constitutional" characteristics.

A constitutional concept is formulated which stresses the correlative importance of dynamic qualities and structural properties of the organism.

SEXUAL CURIOSITY OF CHILDREN

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All children, at one time or another, ask questions concerning a variety of topics. It is therefore not surprising that they also include questions about the topic of sex. These initial inquiries represent a spontaneous reaching out for help, a bringing to a test the effectiveness of verbal formulations (that is, "Is this the best way to say it?") and an attempt to learn how to converse with others. These early experiments in the art of conversation necessarily depend on the development of interpersonal relations, which are of greater significance at the start than the content or meaning of the question itself.

This point is too frequently overlooked when the topic of sex is touched on by the inquiring child. The parent, who has helped the child to express himself on previous occasions, may now become embarrassed, apprehensive or even shocked. The flustered parent may lose sight of the fact that the same child has asked questions concerning other events which have stood out from the daily round of routine experiences.

Children are frequently stimulated to inquire about origins after seeing a litter of kittens for the first time, by the arrival of a puppy in the home, by the presence of a new baby in the neighborhood, by the birth of a sibling or on overhearing a bit of sexual information in the family circle.

An example may help to illustrate this type of normal, healthy curiosity. Mary, aged 6, had been taken to a pet store, where she heard her mother discuss the purchase of a kitten. Mary listened and then asked, "If we buy it, where will they get another? Where do kittens come from?" The mother, who became somewhat embarrassed, replied, "I'll tell you later." Shortly after this incident, Mary saw her father in the bathroom and asked, "Why did Daddy stand up?" Her mother told her that "It's handier because of the clothes." At 6 years 2 months of age, Mary learned that their cat ate birds and wanted to know, "Where do the birds come from?" The mother began to tell her that birds lay eggs, then the mother bird hatches them and the

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father bird feeds them. Mary became bored before the discussion could be completed and said, "I know all about that," then continued to talk about her little garden.

These early orientative tendencies are not "sexual" in the adult sense of the word. The apprehensive parent, who is thinking in terms of possible future sexual experimentation, may try to discourage the child's natural curiosity in this direction by making him aware that certain topics may not be mentioned, that certain parts of the body may not be referred to and that the parent becomes embarrassed by or is frankly critical of such utterances. Although the average child learns to accept the fact that adults have their own peculiar rules and that one of these rules in some homes is that all talk of sex is forbidden, such parental attitudes may help to sensitize the child, so that any reference to this topic will seem to be indecent.

Mrs. M. reported that her 11 year old boy had asked "a lot of questions" but that he had never inquired about origins. She later recalled that he once did say, "Mother, my dog is going to have puppies." She had replied, "All right, Billy, but don't say that to any one else." Mrs. M. also remembered that when Billy was 8 years of age, a 13 year old cousin had told him why a rabbit had a large abdomen and what would soon take place. Billy had immediately gone to his parents and asked them about this newly discovered phenomenon in the presence of two adolescent girl visitors. He was "quieted down" because it was so embarrassing in company. This boy's father is of the opinion that the important thing is "to breed it into them to respect girls; if you do that, you will take care of a lot of trouble later on." But what has been "bred" into Billy is the feeling that he must not ask his parents anything about this "dirty" subject. When he is interviewed at the age of 13, he flushes, shows signs of increasing tension and says that he "doesn't bother much about such things."

The opinion that there might be "a lot of trouble later on" unless certain precautions are taken has been expressed by many of the parents who have been interviewed. These data have been collected since 1937 as part of a study of the development of sexual awareness and sexual attitudes of 200 children, ranging in age from 4 to 12 years. This investigation has been carried out at the Children's Psychiatric Clinic, which is conducted by Dr. Leo Kanner at the Harriet Lane Home, Johns Hopkins Hospital.

The following incidents have been selected from this material in order to indicate some of the sources of these parental misapprehensions. "Mother," remarked a 10 year old girl, "you look like you are going to have a baby?" ("Why?") "Because you are getting so fat." ("How did you hear that?") "That girl in grandfather's apartment

was real fat, and she's got her baby now, and look how thin she is." An 8 year old sister, who was present, added that she had made the same observation. The mother replied, "Yes, it's correct, but don't ever let me hear you say that again. When you get older, I'll explain." This mother went on to say, "I've never heard a word out of them since. It's terrible what they know today. I could have sunk through the floor when they asked me that question."

If this mother could have stopped to think, she might have realized that she had not been asked anything; she had been told something as an accomplished fact. Her own previous experiences had made it difficult for her to discuss such topics with any degree of equanimity. At 10 years of age, this mother had thought that the doctor brought the baby. At 13, when she had menstruated, she had been repeatedly warned to stay away from boys; and when she had asked why, she had been told that "Something might happen. You might get yourself in trouble and bring trouble home to me." At 14, the mother had been embarrassed when the girls at school laughed at her because she had expressed the opinion that "babies came right out of the water." Soon after this she discussed the matter with her married sister and was told in a matter-of-fact manner about the existence of the sexual act. The parental warnings and the embarrassment associated with these early sexual discussions helped to sensitize this mother to the topic of sex.

The futility of this type of vague admonition is illustrated in the next account. When Mrs. W. was 10 years old she believed that "a baby came in an egg like a chicken." She had menstruated at 11 years of age, and soon after the onset of the menses she had been told, "Don't play with boys any more. Don't go into cellars with boys." She inquired, "Why? I played with boys before," and learned that "When you fool with boys you get a baby." She wanted to know how, and the reply was, "Some one else will have to tell you that." This mother recalls, "I thought it was a joke. I wanted a real baby to play with, so I played with the boys more than ever." She remembers how disappointed she had felt when no baby had arrived despite the fact that she had played "as hard as she could."

A parent may smile at the facetiousness of this account of years gone by and pride himself on belonging to a new generation of enlightened parents to whom has been granted a greater freedom in the discussion of these topics. Nevertheless, it is significant that, as a rule, the parents whose sexual questions have been laughed at and who have been shamed are the ones who later give evasive, vague, embarrassed answers to their own children.

The present day tendency to present the child with the analogy of "planting a seed" may also lead to misunderstandings. Such statements usually are not understood by children of preschool age, and not infre-

quently they are misinterpreted by those of early school age. Children belonging to this age group are apt to think of the seed in terms of something which is swallowed and then grows in the stomach, necessitating either evacuation through the bowel or later surgical removal.

David, aged 5, inquired about origins and was told that "the seeds are planted in the mother." He asked how they got in the mother and learned that God put the seeds there. He wanted to know how God put them there, and then, while waiting for the reply, he spontaneously exclaimed, "I know, she swallows them." Nancy was 6 when she inquired, "Was my brother a seed? Jessie (her girl friend) said her little brother was a seed and was planted." "Yes, dear," replied her mother, "it's just like a flower." What did this alert child recall five months later? She expressed herself as being of the opinion that "God brings the babies down from Heaven. He drops them down in the hospital. They sell them there."

William, aged 7, was told that he might harm the dog by playing with her, because there were puppies in her body. He then wanted to know how they got in there and was told about the seed and that babies also grew in mothers. A month later, in keeping with the regular plan of study, he was given an opportunity to express himself in a play-interview concerning his concept of origins. He spoke for a boy doll, saying, "He thinks the mother gets something like a seed, and baby grows in there. The mother sees the seed on the ground and picks it up and swallows it. The baby grows inside the stomach; and when she goes to the bathroom, it comes out of her backside."

Jane was 6 years 3 months of age when her mother told her that "God plants a seed and it grows to be a baby." She was 7 when her baby sister was born. At 8 years 3 months of age, she expressed the following opinion to the physician: "Mothers get babies in hospitals by being operated on. They stay in the hospital for two weeks, because the mother can't walk. Her stomach is still open. God plants a little seed in the mother and the seed grows into a baby. I think it is funny that it does that; that big bump in her stomach, I guess that is the seed."

How does the child begin to orient himself and what does he want to know at various ages? The average child of preschool age thinks in terms of what he sees going on around him. His dependence on the parent, his implicit faith and his lack of contradictory experiences permit him to accept the story of the stork or the idea that the baby is bought in a store. The pregnant mother or neighbor is thought of as having eaten too much and become "too fat." Elizabeth, aged 6, told her eight months pregnant mother, "I wish you would do something about that. You are getting so fat. I don't want to go out with you any more." When her mother informed her that "There is a baby there," Elizabeth exclaimed, "Oh Mother, it isn't!" She was told about "a seed

growing in the mother's heart." There were no further questions until the baby was about 1 month of age; then Elizabeth inquired, "Well, mother, does the stork bring the baby to the mother or does he take it to the doctor?"

The child's own curiosity points in the direction of the mother's body at about the same time he begins to discuss the topic of origins with other children. During this period of socialization, which occurs at about 7 or 8 years of age, the child begins to ask questions about the possibility of the baby being in the body of the mother. He now is interested in learning how the baby leaves the mother's body. Edgar was 5 when he asked, "How do babies grow?" and was told that it was like a flower growing from a bud. At 6, he was visited by twins and asked, "How much does a brother cost? Does it cost more than a sister?" Apparently he had not grasped the analogy with the flower's growth. He was 6 years 8 months of age when he inquired, "What is the first step to have a baby? What do you do to have a baby?" He had passed from one phase of his development to another; he no longer thought that babies could be bought but that the mother had to do something in order to have a baby.

The average child at this age is able to observe and give an account of the changes which occur before and after pregnancy. Arnold, aged 8, remarked to his mother, "My stomach just moves around like a woman who is pregnant," and then asked, "How does the baby get out of the stomach?" At 8 years 11 months of age he could recall, "I noticed a lady with a big stomach (about a year ago) going to the hospital. A lady around our way was skinny and got fat, and then when she had a baby, her stomach got littler. Then I realized babies came from the stomach for sure."

During this phase of development the average boy begins to exchange his sexual information for other sexual facts or fancies. The possession of such knowledge becomes one of the proofs which the boy of 8 or 9 may use in demonstrating to others that he is quite grown-up and knows all about "sex."

This fact may be overlooked by the parent who is still thinking of her 9 year old boy as a child who has been patiently waiting for her to enlighten him. Thus, Mrs. F. asked the physician's advice about whether or not she should tell her son Raymond, aged 9, something about babies, as his oldest sister was about to become a mother. Mrs. F. had been undecided, because her own mother did not think that Raymond was old enough to understand such things.

During the interview Raymond was able to give a detailed account of the sexual act, describing the seminal emission and the manner in which the baby left the mother's body. He had heard other boys dis-

cuss this topic and had accepted what he had learned in a matter-of-fact manner. This mother was told that it would not be advisable at this time to tell Raymond anything about babies. She left, visibly relieved that she did not have to go through this "ordeal."

The child of 9 or 10 years of age is beginning to think in terms of the father's role in the coming of a baby. Richard was 8 years old when he remarked about his mother's pregnancy, saying, "She is getting fat." At 8 years 10 months of age, he was encouraged to read a chapter in a book dealing with sexual information for children. After he had completed it he said, "The kids talk about those things sometimes and get me all mixed up, but I understand how it is now." He then asked what the father had to do with a baby and was told about the ovum and sperm. His only comment was, "That's what I thought."

The first attempts at self observation, coming on at the time when the child is getting acquainted with his body, may lead to a number of inquiries. Donald, aged 4 years 5 months, wanted to know, "What is that little bag (scrotum) for?" and "What is the little hole (navel) for?" Marjorie was 5 years old when she pointed to her nipples and asked, "What is this?" ("A nipple.") She then inquired, "Why do we have these?" At 5 years 8 months of age, Wilbur asked his father of what use was the penis and learned that "It was only nature and it was given to him to pass water." James, aged 6, inquired why he had erections.

At an equally early age children become aware of the differences between their bodies and the bodies of the adults about them. Eugene was 5 when he asked, "What are these?" ("Mother's breasts.") "What are they for?" ("For nursing.") Robert, aged 5, remarked about his mother's breasts, saying, "I am not like that." David wanted to know, at 5 years 6 months of age, what mother's breasts were for. ("They are used to feed babies.") He also asked, "Did I drink out of those when I was little?" ("Yes.") He then inquired, "Is there milk in there now?" ("No, only when there are little babies is there milk in there.") Nancy, at 6 years 5 months of age, asked her mother, "Why aren't my breasts as large as yours?" Frances was 6 years old when she saw the breasts of her 13 year old sister and inquired, "Will I get ones like that?"

The inspection of the bodies of adults gives rise to such questions as that asked by David, aged 6, who wanted to know if he would grow hair under his arms, after seeing the hair in his mother's axillas. Eugene was 6 years old when he asked his mother, "Why is yours got hair? You aren't made like me?" Richard, aged 7 years 10 months, also inquired, "Do you have hair under your arms or down there?" His mother assumed that he had seen the axillas and pubic region of an 11 year old girl playmate. This interest is not restricted to the members of the

opposite sex. Thus Earl was 7 years 6 months old when he and his 6 year old brother began peeping at the father while he was in the shower. He let them come in; they looked at him with some interest and were told that they would grow up and have the same kind of body.

The initial interest in seeing the genitalia of the opposite sex is usually part of the same desire to find out something about the differences which exist between the child's own body and the bodies of others. A number of parents have been misled by medical alarmists to view such activities with consternation and grave apprehensiveness.[1] Mrs. C. referred to her son Robert, 8 years of age, saying, "I hesitate to arouse his curiosity. He might carry it too far." Just previous to being interviewed, Robert and some of his friends, ranging in age from 7 to 10, had taken two 6 year old girls into a tent and asked them to undress. When this incident was reported to the father he "was simply a wreck over it." He waited until he had "calmed down" before he trusted himself to discuss it with Robert. During the play-interview this boy spoke for each of a number of boy dolls and said that they were interested in undressing a girl "in order to see what she looks like in front." He went on to say that several of his boy friends had had an opportunity to see a girl's genital, and he also wanted to see what it was like.

This type of experience does not stimulate the average child to explore his environment further sexually. In a previous paper [2] the statement was made that the average child of 5 or 6 who has had an opportunity to observe genital differences can say that the boy has a "straight one and the girl ain't" or "a boy's sticks out and a girl's don't." This is as much a fact as any other fact which the child has experienced, and he can report what he has seen without any feeling of embarrassment. It is the name or label which he finds great reluctance in divulging. This name may be as innocent as the words "dew drop," "Teddy bear," "train" or "piece of string"; nevertheless, the child becomes restless, bites his lips or hangs his head and refuses to speak. Not less than 61 different names have been offered by 200 children. It is not surprising that Morton, aged 7, could say that "There are so many names for that thing, I don't know what name I should say." His own term for the genital was "kisser," but he added that his mother had warned him not to say such "dirty" words.

Nevertheless, despite these man-made verbal barriers, children can present their unbiased opinions when they are given an opportunity to express themselves in experimental play situations,[3] where they can

1. Kanner, L.: Infantile Sexuality, J. Pediat. **4**:583-608 (Oct.) 1939.

2. Conn, J. H.: Sex Attitudes and Sex Awareness in Young Children, Child Study **16**:86-87 and 106-107 (Jan.) 1939.

3. Conn, J. H.: The Child Reveals Himself Through Play, Ment. Hyg. **23**: 46-69 (Jan.) 1939; The Play-Interview: A Method of Studying Children's Attitudes, Am. J. Dis. Child. **58**:1199-1214 (Dec.) 1939.

feel relatively free from embarrassment, by speaking for one of a number of dolls, as if it were doing the talking. These clinical facts, when combined with a record of the opportunities for sexual experimentation and viewed from the perspective of the child's life history, have made it possible to come to the conclusion that "the healthy, normal, average child accepts the difference in urination posture and in the genital of the opposite sex [4] calmly, as a given reality, without struggle, without a feeling of superiority in the male or inferiority in the female." [5]

Healthy children are not as easily upset as some theorists would lead us to believe.[6] Children pass from one experience to another, assimilating and synthesizing their sexual experiences as they do with other issues of everyday living. An excellent example of this type of wholesome progression is presented by Florine. This child was 3 years old when she was permitted to go to the bathroom with a boy playmate of the same age. She reacted to this experience by inquiring, without any evidence of perturbation, "Why can a boy stand up and I can't?" She was told that "Boys are made different." At 5 years Florine informed her sister, aged 3, when the same question came up, that "Boys are different." At 8, while in the tub, she asked, "What are these?" ("Breasts.") "Why do we have these?" ("To nurse the baby.") "Why do ladies have big breasts?" ("As they grow the chest grows and they get bigger there.") A few days later, while bathing, she asked, "What do you call that?" ("The vagina.") The mother recalled that "she seemed curious to know the names, but when she learned them she didn't seem to bother any more."

At 9, Florine wanted to know, "Where do kittens come from?" She was told they came from the mother cat. At 10, she asked her mother if it were really true that the lady in the next street was going to have a baby and that the baby was in the stomach. She had been discussing this topic with her girl friend. She was told, "All babies come like that. You did too." Florine then asked, "Why didn't you tell me that before?" The mother replied, "I didn't think that you were old enough. When you are in the first grade you learn easier things, then later you learn harder things." In this manner Florine was encouraged to express herself and learned by example rather than by precept, the way in which a parent should reply to a child's sexual questions.

It is important to emphasize that this degree of self expression in regard to the topic of sex is relatively uncommon. Children ask remark-

4. Conn, J. H.: Children's Reactions to the Discovery of Genital Differences, read at the meeting of the American Psychiatric Association, Chicago, May 11, 1939, to be published.

5. Conn, J. H., and Kanner, L.: Children's Awareness of Sex Differences, to be published.

6. Conn, J. H.: Factors Influencing Development of Sexual Attitudes and Sexual Awareness in Children, Am. J. Dis. Child. **58**:738-745 (Oct.) 1939.

ably few sexual questions. This fact stands in direct contrast to the opinions of many parents who have been led to believe that unless special precautions are taken to check their children's sexual curiosity there will follow a veritable deluge of embarrassing inquiries.

A statistical evaluation of the sexual questions contributed by the 200 children in this study, representing all the social stratums in approximate proportion to their distribution in the community, reveals that the average child from the age of 4 to the age of 12 asks his parents less than 2 such questions. A similar finding has been reported by Hattendorf,[7] who has collected the sexual questions of nearly 2,000 children.

Almost one quarter of all the inquiries which were reported in this study occurred at the age of 6, and slightly more than one half of the entire number of questions were offered in the early school years from 6 to 8. There were questions from 71 per cent of the boys and 70 per cent of the girls. Of the boys of superior intelligence (intelligence quotients from 111 to 140), 85 per cent asked questions, while 73 per cent of those with average intelligence (intelligence quotients from 91 to 110) and only 62 per cent of the boys with lesser degrees of intelligence contributed questions. Questions were asked by 83 per cent of the girls of average intelligence and by 66 per cent of those of superior intelligence; only 52 per cent of the lowest group (intelligence quotients from 71 to 90) asked sexual questions. As a group, the more intelligent children asked sexual questions more frequently, and individually they offered more questions per child. Even in this superior group (intelligence quotients from 111 to 140), the average number of sexual inquiries did not rise above 2.0 questions for each child. The median intelligence quotient for the total number of children was 95.2.

It is important to call attention to the fact that 29 per cent of the 128 boys and 30 per cent of the 72 girls were reported as not having inquired about sexual topics. Forbidding parental attitudes, the lack of opportunity for sexual play and sexual discussion with other children, the factor of intelligence and the fact that most immature children of average or even superior intelligence do not ask sexual questions may help to explain these observations.

The facts speak for themselves. Parents must learn that they have been frightened by a few vociferous psychologists living in academic seclusion and by a handful of psychiatrists who have been blinded by a priori theorizing into viewing with alarm the future of the child who has not been "completely" sexually enlightened. Children do not ask for such "complete" explanations. The scope of their sexual interests, like the growth of their appetites and heights, increases with the years.

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7. Hattendorf, K. W.: A Study of the Questions of Young Children Concerning Sex, J. Social Psychol. **3**:37-65 (Feb.) 1932.

The sexual information that they require cannot be administered in one dose any more than can the vitamins they require.

There is no such thing as not giving sexual instruction. Most of the significant sexual attitudes are presented to children in an unverbalized form. These attitudes and standards, like so many songs without words, are the melodies which linger on. Parents have worried too much about giving children the proper answers and not enough about becoming the proper persons. Let each parent do his work in his own way. Let the easily embarrassed parent remain embarrassed. (He will anyway, no matter what is said here.) The apprehensive parent will continue to be fearful and oversolicitous. Perhaps it is best for those who are hesitant and relatively inarticulate to remain silent.

Not every parent can hope to attain the dissociated, scientifically objective attitude of the trained physician, nor is it necessary. Nevertheless, every parent can become sufficiently child minded to know that whenever he is asked a question and replies in effect, "Run away, little man, and play," he not only discourages the child's questions on this particular topic but overlooks an opportunity to learn something about the child.

The parent who takes the time to ask, "Why do you want to know that?" or "What is your opinion about that?" will be enlightened concerning the nature of the information which is being sought, the degree of sexual interest and the level of understanding at that specific age and for that particular child. Only the child himself can give information concerning what he actually wants to know and how much he can absorb out of that which he has been told.

Children who are encouraged in this manner to express themselves are not stimulated to explore their environment sexually. Their inquiries about concrete events of everyday life may serve as a basis for the presentation of a necessary sexual vocabulary. But no series of scientific terms can "immunize" a child against the inevitable language of the street. The child may need both in order to become an effective member of his group.

All parents might profit if they could stop being fortune tellers and cease peering into the future for the purpose of preventing calamities which probably never will happen. In any case, the most apprehensive parent can learn to appreciate the fact that the child is not as fragile a creature as some persons make him out to be. He should remember that in the serious business of life, collections of words count for much less than training for effective living. The parent in the average home, who is doing his best to give the child an opportunity to express himself and to share in the common experiences of everyday life, may justifiably feel that he has made a most significant contribution to the health and happiness of his children.

BLOOD LIPID PARTITION IN HYPOTHYROIDISM OF CHILDHOOD

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The diagnosis of severe hypothyroidism in children resulting from congenital absence or deficiency of the thyroid gland usually presents little difficulty. The neonatal history, the delay in physical and mental development and the characteristic clinical features coupled with delay in development of centers of ossification and elevation of the concentration of blood cholesterol leave little doubt as to the nature of the ailment. In the typical case, determination of the basal metabolic rate may be corroborative.

A more perplexing problem is encountered in the diagnosis of mild hypothyroidism. Many of the familiar clinical criteria on which one relies for diagnosis may be equivocal or even absent. Mental and physical development may be only slightly retarded. Determination of the basal metabolic rate may not be possible because of the age of the patient or lack of cooperation.

It has been stated that retardation in osseous development is the most consistent finding in children with hypothyroidism.[1] However, normal development before the onset of the disease frequently masks this characteristic feature of acquired hypothyroidism. Thus, delay in skeletal development may not become evident until the disease is advanced. Moreover, conditions other than disease of the thyroid may be responsible for delay in the appearance of centers of ossification.[2]

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1. Molitch, M., and Poliakoff, S.: Subclinical Hypothyroidism in Children, Endocrinology **20**:816, 1936.

2. Francis, C. C.: Factors Influencing Appearance of Centers of Ossification During Early Childhood, Am. J. Dis. Child. **57**:817 (April) 1939.

Corroborative evidence which is consistently present and is easily obtained would therefore be of great advantage in making the diagnosis. This has hitherto not been available. It is our belief that determination of the concentration of the total serum lipids may prove such a criterion.

Alteration of the concentration of blood lipids as a result of hypothyroidism has long been recognized, but this has been measured in most instances by a determination of the level of blood cholesterol. It has been stated by Epstein and Lande [3] that estimates of total cholesterol may be used as a measure of the total fat content of the blood, since the cholesterol concentration in the blood "goes hand in hand with that of the other fats." It is generally believed that the level of blood cholesterol is elevated in most cases of hypothyroidism. On the other hand, normal concentrations of cholesterol have been reported in undoubted cases.[4] Experimentally, thyroidectomy in the dog produces hypercholesteremia.[5] The literature is extensive and need not be further reviewed. Variations in normal cholesterol concentration in the blood have been reported over ranges as wide as 109 to 376 mg. per hundred cubic centimeters by Page and associates [6] and 132 to 392 mg. per hundred cubic centimeters by Sperry.[7] Cholesterol values up to 265 mg. per hundred cubic centimeters were found in normal persons by Man and Gildea.[8] It is evident that in the diagnosis of hypothyroidism emphasis on a single elevation of the concentration of blood cholesterol may be misleading.

A significant correlation has been demonstrated [9] between the concentration of blood cholesterol and changes in the basal metabolic rate

3. Epstein, A. A., and Lande, H.: Studies on Blood Lipoids: I. The Relation of Cholesterol and Protein Deficiency to Basal Metabolism, Arch. Int. Med. **30**:563 (Nov.) 1922.

4. (*a*) McGee, L. C.: Blood Cholesterol in Disturbances of the Basal Metabolic Rate, Ann. Int. Med. **9**:728, 1935. (*b*) Boyd, E. M., and Connell, W. F.: Plasma Lipids in the Diagnosis of Mild Hypothyroidism, Quart. J. Med. **6**:467, 1937.

5. Schmidt, L. H., and Hughes, H. B.: The Free and Total Cholesterol Content of Whole Blood and Plasma as Related to Experimental Variations in Thyroid Activity, Endocrinology **22**:474, 1938.

6. Page, I. H.; Kirk, E.; Lewis, W. E., Jr.; Thompson, W. R., and Van Slyke, D. D.: Plasma Lipids of Normal Men at Different Ages, J. Biol. Chem. **111**:613, 1935.

7. Sperry, W. M.: The Relationship Between Total and Free Cholesterol in Human Blood Serum, J. Biol. Chem. **114**:125, 1936.

8. Man, E. B., and Gildea, E. F.: Variations in Lipemia of Normal Subjects, J. Biol. Chem. **119**:769, 1937.

9. Hurxthal, L. M.: Blood Cholesterol in Thyroid Disease: Analysis of Findings in Toxic and Nontoxic Goiter Before Treatment, Arch. Int. Med. **51**:22 (Jan.) 1933.

in disease of the thyroid. The cholesterol concentration is dependent not on the metabolic rate but on the action of the thyroid hormone. Alterations in the basal metabolic rate occasioned by dinitrophenol were not accompanied by corresponding changes in the cholesterol level.[10] This relation between basal metabolic rate and cholesterol level may be absent (McGee [4a]; Grabfield and Campbell [11]). In some quarters the basal metabolic rate is considered a more reliable criterion of diminished function of the thyroid gland than estimation of the concentration of blood cholesterol.[12]

Little is known regarding the effect of hypothyroidism on the concentration of other lipid components of the blood. In an attempt to avoid the difficulties of analysis for cholesterol, Chamberlain, Jacobs and Butler [13] determined the amount of total blood fat by means of the hemolipocrit method of Rückert,[14] which is a volumetric method for the rapid analysis of fat in small samples of blood. They described an inverse relation between the amount of total blood fat and thyroid function. Aside from any criticism of the method of analysis, their results are inconclusive, since in only 2 of their patients was the concentration of total lipids elevated. In 1, a lowering of the concentration of total lipids was observed after thyroid medication. They considered a concentration of total blood lipids of 700 mg. per hundred cubic centimeters as the upper limit of normal.

Boyd and Connell [12a] found no consistent increase in the concentration of plasma lipids in untreated adults with hypothyroidism but noted a moderate reduction after treatment with thyroid. Thus, the lipid concentrations in their patients with hypothyroidism were essentially within normal limits, both before and after thyroid therapy. These limits had been previously determined by Boyd in an analysis of 118 normal subjects.[15] In a later communication,[4b] they described a mild

10. Cutting, W. C.; Rytand, D. A., and Tainter, M. L.: Relationship Between Blood Cholesterol and Increased Metabolism from Dinitrophenol and Thyroid, J. Clin. Investigation **13**:547, 1934.

11. Grabfield, G. P., and Campbell, A. G.: A Note on the Relation Between Blood Cholesterol and the Basal Metabolic Rate, New England J. Med. **205**:1148, 1931.

12. (*a*) Boyd, E. M., and Connell, W. F.: Thyroid Disease and Blood Lipids, Quart. J. Med. **5**:455, 1936. (*b*) Hellwig, C. A.: Laboratory Aids in Hypothyroidism, J. Kansas M. Soc. **37**:506, 1936.

13. Chamberlain, C. T.; Jacobs, S., and Butler, M. F.: Total Blood Fat Determination as an Index of Thyroid Function, Am. J. M. Sc. **191**:66, 1936.

14. Rückert, W.: Eine Einfache volumetrische Mikrobestimmung des Blutfettes (Lipokritverfahren), Klin. Wchnschr. **10**:1853, 1931.

15. Boyd, E. M.: The Interrelation of Blood Lipids, Canad. J. Research (Sect. D) **15**:1, 1937.

elevation in the concentrations of all lipid fractions except neutral fats in adults with hypothyroidism. They considered evidence of improvement in symptoms in their patients after thyroid therapy proof of the existence of hypothyroidism. The elevation of the concentration of plasma lipids was held to be a verification of the diagnosis; yet only 5 of their patients showed an elevation of the level of total lipids beyond the range of 381 to 752 mg. per hundred cubic centimeters, which Boyd had previously established as normal. In his study of the normal lipid concentration in the blood, Boyd [15] maintained that in order to interpret the significance of a single analysis this concentration should be compared with the range found in 95 per cent of normal subjects. When a group of values is to be compared with the normal, the range in two thirds of normal persons should be used as a standard. In all their patients with hypothyroidism, Boyd and Connell [4b] found an elevation of the concentration of plasma lipids beyond the range expected in two thirds of normal subjects. This would verify their contention that in patients with hypothyroidism, as a group, there is an elevation in concentration of blood lipids beyond the expected normal range. However, in only 56 per cent of their patients did the level of total plasma lipids exceed the range of 95 per cent of the normal subjects in Boyd's series. Because of this marked overlapping between the ranges of normal and abnormal lipid concentrations, the question arose whether analyses for concentrations of total blood lipids afforded reliable evidence of the existence of hypothyroidism in more than 56 per cent of the patients studied. It was therefore considered advisable to study further the blood lipid partition of patients with undoubted hypothyroidism, in order to demonstrate the value of the determination of lipid concentrations in the diagnosis of this condition. All the observations described in this report were made on children.

METHOD

Seventy-four patients were studied for evidence of hypothyroidism. They were all between the ages of 4 and 15 years. Our investigation included a careful history and physical examination. Roentgenograms of the wrists and sella turcica were taken routinely. The basal metabolic rate was determined whenever possible, and when indicated a dextrose tolerance test was done. The intelligence quotient of the patient was obtained when feasible. In addition, studies were made of the blood lipid partition. These were confined to determinations of the concentrations of total lipids, total cholesterol, free cholesterol and lipid phosphorus. In 12 of the cases the diagnosis of cretinism had been established before these studies were begun. Because thyroid therapy had already been instituted in these cases, concentrations of blood lipids were determined while the patients were under treatment and also after the administration of thyroid had been discontinued for from four to ten weeks. In 5 other cases a definite diagnosis of acquired hypothyroidism was established while this study was in progress. In these, concentrations

of blood lipids were determined before treatment and also sometime after therapy had been introduced. In all 17 cases the diagnosis was corroborated by the favorable response of the patient to thyroid therapy. A description of the patients and the criteria on which the diagnosis was based are included in table 1.

In this communication we are concerned only with the blood lipid partition of patients with undoubted hypothyroidism. The results of the analyses of the blood lipid partition of the remaining patients and their significance in the differential diagnosis of borderline hypothyroidism will be reported at a later date.

In the analyses of the blood lipid partition the following technic was used:

In preparation of the lipid extracts, the methods of Kirk, Page and Van Slyke [16] were followed.

The content of total serum lipids was determined gravimetrically by evaporating the alcohol-ether extract of 2.5 to 4 cc. of serum to dryness at a temperature under 60 C., extracting the residue with purified petroleum benzine U. S. P. (boiling point between 35 and 60 C.), filtering into a weighed 50 cc. beaker, evaporating the petroleum benzine filtrate to dryness at a temperature under 60 C., and finally drying the residue in a vacuum desiccator for one hour. The beaker was then weighed and the weight of the lipid residue determined. The residue was taken up in 10 cc. of benzene, and aliquots were used for the subsequent determinations of total cholesterol, free cholesterol and lipid phosphorus.

The total cholesterol content was determined by evaporating to dryness 1 cc. of the aforementioned benzene solution, dissolving the residue in 1 cc. of glacial acetic acid, adding 2 cc. of acetic anhydride and 0.1 cc. of concentrated sulfuric acid and allowing the color to develop for twenty-seven and a half minutes. The color was then read against a standard containing 0.6 mg. of cholesterol.

The concentration of free cholesterol was determined on 2 cc. of the benzene solution according to the procedure of Drekter, Sobel and Natelson.[17]

The content of lipid phosphorus was determined by a modification of the method of Fiske and Subbarow.[18] Two cubic centimeters of the benzene extract was evaporated to dryness in a combustion tube; 1.2 cc. of five times normal sulfuric acid, 0.3 cc. of concentrated nitric acid and two glass beads were added. The tube was gently heated with a microburner, which was kept at least 2 cm. away from the bottom of the tube, until the solution was perfectly clear, more nitric acid being added, a drop at a time, if necessary. The flame was lowered, and the tube was heated until white fumes appeared; it was then heated for ten minutes longer. The tube was cooled for five minutes, and 1 cc. of a 15 per cent solution of sodium sulfate was added to remove the excess nitric acid. The tube was gently heated two minutes longer to remove any sulfur dioxide present. The contents were cooled and diluted to 6 cc., and 5 cc. was removed into a 10 cc. volumetric flask. From this point the colorimetric procedure of Fiske and Subbarow was followed.

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16. Kirk, E.; Page, I. H., and Van Slyke, D. D.: Gasometric Microdetermination of Lipids in Plasma, Blood Cells and Tissues, J. Biol. Chem. **106**:203, 1934.

17. Drekter, I. J.; Sobel, A. E., and Natelson, S.: Fractionation of Cholesterol in Blood by Precipitation as Pyridine Cholesteryl Sulphate and Cholesterol Digitonide, J. Biol. Chem. **115**:391, 1936.

18. Fiske, C. H., and Subbarow, Y.: Colorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375, 1925.

TABLE 1.—*Data for Seventeen Children Treated for Hypothyroidism*

Patient	Age	Developmental History		Clinical Signs and Symptoms of Hypothyroidism	Basal Metabolic Rate	Skeletal Development	Blood Cholesterol While Not Under Treatment, Mg. per 100 Cc.	Results of Thyroid Therapy	Diagnosis
		Physical	Mental						
S. R.	9 yr. 5 mo.	Delayed	Delayed	Characteristic	—34	Delayed	415 408	Marked improvement	Congenital hypothyroidism
I. S.	4 yr.	Delayed	Delayed	Characteristic †	....	Normal *	456	Marked improvement	Congenital hypothyroidism
A. A.	7 yr.	Delayed	Delayed	Characteristic	—21	Normal *	466	Marked improvement	Congenital hypothyroidism
L. S.	6 yr. 8 mo.	Normal	Normal	Characteristic	—22	Normal §	445	Improvement	Acquired hypothyroidism
A. D.	11 yr.	Delayed	Delayed	Characteristic	—42	Delayed	560 602	Marked improvement	Congenital hypothyroidism
R. B.	4 yr. 6 mo.	Normal	Normal	Characteristic	....	Delayed after 3 yr.	395 449	Marked improvement	Acquired hypothyroidism
P. D.	13 yr.	Normal	Normal	Characteristic	—21	Normal §	...	Improvement	Acquired hypothyroidism
H. N.	6 yr. 6 mo.	Delayed	Delayed	Characteristic	....	Delayed	239	Marked improvement	Congenital hypothyroidism
B. L.	10 yr.	Delayed	Delayed	Characteristic	—32	Delayed	...	Marked improvement	Congenital hypothyroidism
L. E.	15 yr. 6 mo.	Delayed	Delayed	Characteristic †	2 *	Normal *	320	Marked improvement	Congenital hypothyroidism
S. C.	13 yr. 6 mo.	Normal	Normal	Characteristic †	—23	Normal §	343	Marked improvement	Acquired hypothyroidism
B. F.	11 yr. 6 mo.	Normal	Normal	Characteristic	—13	Delayed	287	Marked improvement	Acquired hypothyroidism
W. S.	12 yr.	Delayed	Delayed	Characteristic ‡	—17	Delayed	260	Marked improvement	Congenital hypothyroidism
A. F.	15 yr. 6 mo.	Delayed	Delayed	Characteristic	....	Delayed	337	Marked improvement	Congenital hypothyroidism
D. G.	14 yr.	Delayed	Delayed	Characteristic	— 9	Delayed	459	Marked improvement	Congenital hypothyroidism
M. S.	9 yr.	Delayed	Delayed	Characteristic † ‡	— 1*	Delayed	300	Marked improvement	Congenital hypothyroidism
C. S.	5 yr.	Normal *	Normal *	Characteristic	....	Normal *	...	Marked improvement	Congenital hypothyroidism

* This was while being treated with thyroid.
† Electrocardiographic changes of hypothyroidism were also present.
‡ Osteochondrosis of the capital femoral epiphysis was also present.
§ The skeletal development appeared normal because the disease was of recent origin.

Few determinations of the normal levels of blood lipids in children have been reported. For the most part these have been limited to the estimation of cholesterol content.[19] Hansen [20] determined the concentrations of cholesterol and fatty acids in normal children under 2 years of age and in those from 2 to 15 years old in order to compare them with the concentrations found in the blood of eczematous children. Wilson and Hansen [21] determined the concentrations of serum lipids of children and young adults and have found the average for total blood lipids to be 675 mg. per hundred cubic centimeters, with a range of from 433 to 810 mg. per hundred cubic centimeters. Chaikoff, Smyth and Gibbs [22] determined the values for lipids in whole blood of 23 normal children, in order to compare them with values obtained in diabetic children. They found the range to be from 417 to 595 mg. per hundred cubic centimeters.

In order to establish the normal values for blood lipids for the method of analysis used in our laboratory, blood samples were taken from 54 normal ambulatory children who ranged in age from 2 months to 16 years. Analyses were made early in the morning before breakfast. There was not considered to be any significant difference in the concentrations of the blood lipids in boys and girls. This lack of variation with the sex of the subject has been borne out by Offenkranz and Karshan [19a] in children and by Boyd [15] in adults.

RESULTS

Normal Children.—In table 2 figures for the serum lipid partition of normal children are presented. These children had been under the supervision of a trained pediatrician and were considered normal. The range of values for total lipids in our analyses was from 363 to 848 mg. per hundred cubic centimeters (chart 1). These values are slightly higher than those reported by Boyd [15] but agree with those obtained by Page and his co-workers [6] in adults and by Wilson and Hansen [21] in children and young adults. The total amount of cholesterol ranged from 107 to 299 mg. per hundred cubic centimeters. These values are higher

19. (*a*) Offenkranz, F. M., and Karshan, M.: Serum Cholesterol Values for Children, Am. J. Dis. Child. **52**:784 (Oct.) 1936. (*b*) Gørtz, S.: Blood Cholesterol Determinations as an Auxiliary Means of Diagnosticating Myxoedema in Children, Acta pædiat. **29**:553, 1937.

20. Hansen, A. E.: Serum Lipids in Eczema and in Other Pathological Conditions, Am. J. Dis. Child. **53**:933 (April) 1937.

21. Wilson, W. R., and Hansen, A. E.: Study of the Serum Lipids by a Microgravimetric Technique, J. Biol. Chem. **112**:457, 1936.

22. Chaikoff, I. L.; Smyth, F. S., and Gibbs, G. E.: The Blood Lipids of Diabetic Children, J. Clin. Investigation **15**:627, 1936.

than those described by Gørtz [19b] but not as high as those found by Page and his co-workers,[6] or by Sperry.[7] They compare favorably with the findings of Man and Gildea.[8]

TABLE 2.—*Blood Lipid Partition of Normal Ambulatory Children*

Case	Age in Years	Weight in Pounds	Height in Inches	Difference Between Actual and Ideal Weights, Percentage	Total Lipids, Mg. per 100 Cc.	Total Cholesterol, Mg. per 100 Cc.	Free Cholesterol, Mg. per 100 Cc.	Percentage Free in Total Cholesterol	Lipid Phosphorus, Mg. per 100 Cc.
1	12	132	61¼	+35	363	107	27.0	25.2	4.3
2	9	61	54¾	−10	391	130	36.3	29.0	3.7
3	16	150	68	+10	403	120	23.8	19.8	4.7
4	16	133	68½	− 4	457	142	28.7	20.2	5.1
5	16	157	70¾	+ 4	460	124	25.0	20.2	5.6
6	14	89½	61¾	−12	467	175	32.9	18.8	5.8
7	1	24	29	+14	467	150	33.5	21.1	5.3
8	12	94½	62	− 7	482	148	34.1	23.0	5.6
9	16	160	69½	+11	483	140	28.0	20.0	5.0
10	13	119½	63	+12	494	155	46.7	30.0	5.9
11	2½	28	..	− 5	495	210	56.9	27.1	7.5
12	15	100	61	+ 0	503	178	34.8	19.6	5.6
13	15	127	64	+10	509	217	42.4	19.1	4.7
14	11	96½	58¾	+ 9	509	175	31.7	18.1	5.7
15	4½	42	44	+ 2	517	183	36.3	20.0	5.7
16	9 mo.	17½	30	−17	520	139	33.3	25.4	5.5
17	3	67	41	+83	532	259	40.5	15.6	7.2
18	9	79½	55	+10	538	161	40.0	24.9	4.8
19	11	77½	57¾	− 7	546	200	40.0	25.0	5.7
20	12	101	58½	+16	556	191	42.9	22.5	6.7
21	15	94½	59½	+ 2	557	199	41.5	20.9	6.0
22	13	124	64¼	+12	568	174	49.6	28.5	6.7
23	14	107	61¼	+ 9	573	183	42.5	23.2	6.7
24	14	91	63¼	−16	588	175	48.8	27.9	7.0
25	15	113	62¾	+ 4	582	190	38.4	20.2	6.3
26	14	82	58¼	− 5	595	189	44.7	23.7	6.7
27	13	83½	57½	+ 0	615	190	52.1	27.4	7.0
28	2½	32¾	....	+11	615	207	56.3	27.2	7.2
29	7	45	47	−10	622	207	52.5	25.4	6.5
30	14	101	59¾	+ 7	641	208	52.9	25.0	8.8
31	11	75½	56½	− 4	661	209	60.2	28.8	7.2
32	10	82	56¼	+ 6	662	204	51.4	25.2	7.4
33	5½	42½	43¼	+ 4	663	227	66.4	29.2	8.1
34	10	63	52¾	− 4	665	254	57.7	28.3	7.9
35	11	72	56¾	−11	668	202	44.0	21.8	7.4
36	9	72	52½	+12	671	234	65.7	28.1	8.2
37	5	36¼	41½	− 5	672	233	78.8	33.8	8.5
38	8	....	....	....	674	203	48.9	24.1	8.6
39	13	98½	60¾	0	677	211	55.8	26.4	8.1
40	8	....	....	..	690	190	46.7	24.6	7.4
41	2 mo.	10	21	0	706	165	44.8	27.1	7.7
42	13	96	61	0	708	220	65.6	27.0	8.7
43	8	....	....	..	708	181	47.0	26.0	7.3
44	8	....	....	..	733	194	46.8	24.3	9.1
45	16	150	67¼	+12	741	186	41.0	22.0	8.4
46	11	88	59	0	754	228	50.0	22.0	8.3
47	6	36	43¼	−12	763	208	61.7	29.7	7.8
48	3½	37¼	40	+ 5	802	299	77.0	25.8	9.4
49	10	70	53½	+ 3	804	240	53.2	22.2	9.1
50	8	..	....	....	806	190	56.8	29.9	9.4
51	10	77	52½	+20	812	229	56.0	24.4	10.4
52	2½	28½	....	− 3	814	200	60.0	30.0	7.8
53	4	52	42	+33	827	267	65.0	24.4	9.8
54	4 mo.	15½	24½	+10	848	196	52.4	53.4	8.5
Mean values					614	193	47.2	24.5	6.7
Standard mean deviation					103	28	10.1	....	1.3

In general, a direct correlation was found to exist between the levels of total lipids and total cholesterol. This relation may be expressed mathematically in terms of its correlation coefficient. This, when cal-

culated according to the method of Fischer,[23] was found to be 0.734. A direct, but not absolute, correlation is thus indicated, which is also demonstrated graphically in chart 2.

The proportion of free to total cholesterol varied from 19.1 to 30.0 per cent, with an average of 24.5 per cent. These results are similar to

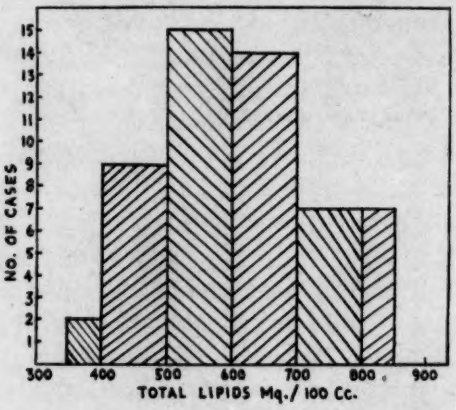

Chart 1.—The range of concentrations of total serum lipids in normal ambulatory children.

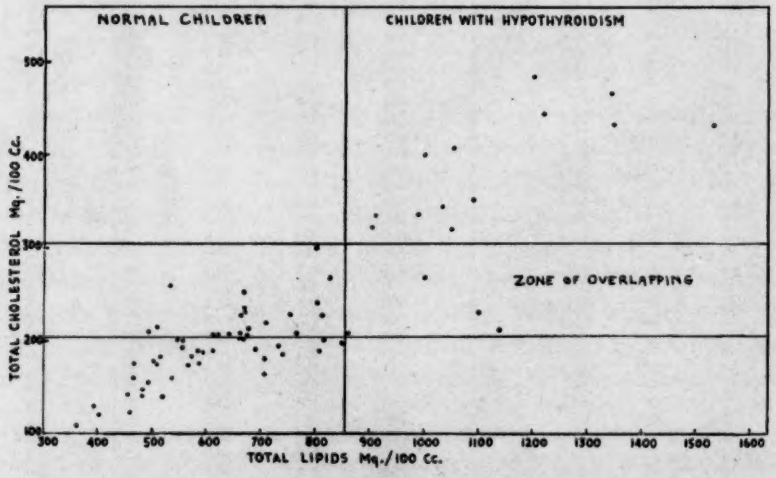

Chart 2.—Correlation between concentrations of total serum lipids and total cholesterol in normal children and in children with hypothyroidism.

those of Sperry [7] and tend to corroborate his contention that the ratio of free to total cholosterol varies in normal persons over a fairly limited

23. Fischer, R. A.: Statistical Methods for Research Workers, ed. 6, London, Oliver & Boyd, 1936.

range. In chart 3 the values for free cholesterol have been plotted against those for total lipids. The corrleation here is noted to be even more direct than that between the concentrations of total cholesterol and total lipids. This is emphasized by the correlation coefficient of 0.927.

The concentration of lipid phosphorus ranged from 3.7 to 10.4 mg. per hundred cubic centimeters. In over 95 per cent of the patients this value was found to be between 0.9 and 1.3 per cent of the concentration of total lipids. The close correlation between the concentrations of lipid phosphorus and total lipids is borne out mathematically by the correlation coefficient of 0.884. This straight line correlation between the two is also demonstrated in chart 4.

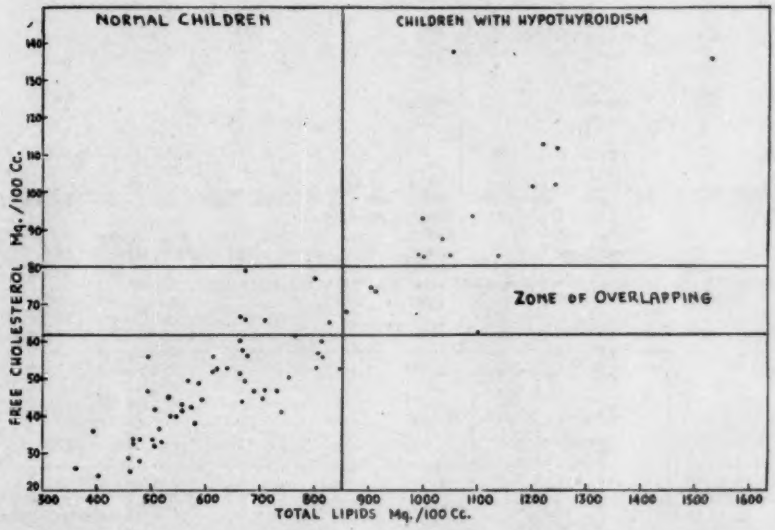

Chart 3.—Correlation between concentrations of total serum lipids and free cholesterol in normal children and in children with hypothyroidism.

Children with Hypothyroidism.—In table 3 figures for the blood lipid partition of 17 patients with typical hypothyroidism are presented. Clinical signs and symptoms of the disease were present in all patients, and a characteristic history and confirmatory laboratory criteria were obtained. Further evidence of hypothyroidism was provided by the uniformly favorable response to thyroid therapy and by the return of symptoms of hypothyroidism whenever therapy was discontinued. There were 12 cases of congenital and 5 of acquired hypothyroidism. The values for total blood lipids are set down in descending order. These were elevated in all cases and ranged from 1,531 to 854 mg. per hundred cubic centimeters, with a mean value of 1,104 mg. per hundred cubic

centimeters (chart 5). In no case did these values overlap the previously established upper limit of normal. This cannot be said regarding the concentration of total cholesterol. In 4 of the 17 patients the cholesterol level was within what is usually considered the normal range. In chart 2, the values for total cholesterol have been plotted against those for total

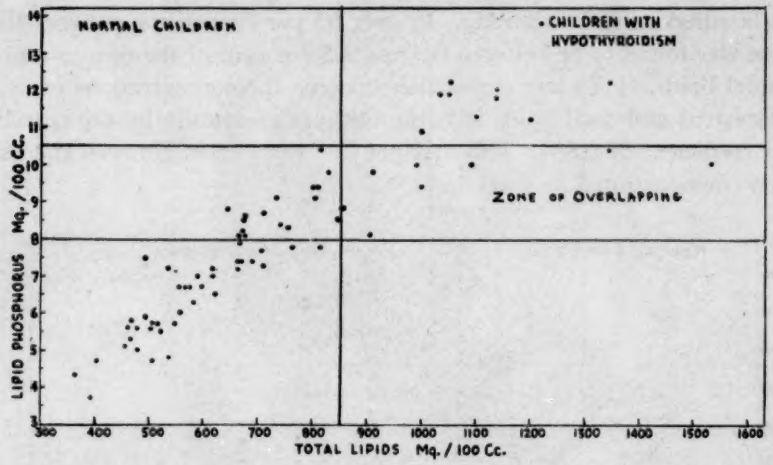

Chart 4.—Correlation between concentrations of total serum lipids and lipid phosphorus in normal children and in children with hypothyroidism.

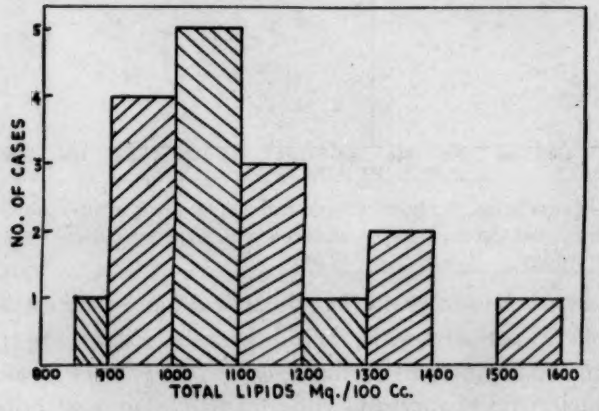

Chart 5.—The range of concentrations of total serum lipids in children with hypothyroidism.

lipids. It is evident that although there is a direct correlation between the concentrations of total lipids and cholesterol, there is a considerable spread about the mean. The wide zone of overlapping may be noted between the cholesterol levels of 200 and 300 mg. per hundred cubic centimeters, so that in 4 cases of hypothyroidism the cholesterol values

fall within this zone. Since in every patient with hypothyroidism in our series the concentration of total lipids exceeded that for normal children, there is graphically revealed the comparative inadequacy of the estimation of the content of total cholesterol in the diagnosis of hypothyroidism as compared with that of total lipids. In the 4 patients with hypothyroidism with normal cholesterol values there was no evidence of anemia, malnutrition, hepatic disease or other conditions to account for these findings.

The values for free cholesterol in these children ranged from 62.5 to 138.0 mg. per hundred cubic centimeters. This constitutes from 20.9 to 33.7 per cent of the concentration of total cholesterol in all but 1

TABLE 3.—*Blood Lipid Partition in Untreated Hypothyroidism of Childhood* *

Patient	Diagnosis	Blood Lipid Partition in Mg. per 100 Cc.				
		Total Lipids	Total Cholesterol	Free Cholesterol	Percentage Free in Total Cholesterol	Lipid Phosphorus
S. R.	Cretinism	1,531	431	136.0	31.5	10.0
I. S.	Cretinism	1,347	433	112.0	25.8	12.2
A. A.	Cretinism	1,342	466	102.0	26.2	10.4
L. S.	Acquired hypothyroidism	1,221	445	113.0	25.4	13.3
A. D.	Cretinism	1,198	485	101.5	20.9	11.2
R. B.	Acquired hypothyroidism	1,138	211	83.0	39.3	11.8
P. D.	Acquired hypothyroidism	1,100	230	62.5	27.2	11.3
H. N.	Cretinism	1,000	353	93.2	26.4	10.0
B. L.	Cretinism	1,053	409	138.0	33.7	12.2
L. E.	Cretinism	1,050	320	82.8	25.9	11.9
S. C.	Acquired hypothyroidism	1,034	343	87.5	25.5	11.9
B. F.	Acquired hypothyroidism	1,001	269	82.9	30.8	10.9
W. S.	Cretinism	999	400	93.0	23.2	9.4
A. F.	Cretinism	990	337	83.3	24.7	10.0
D. G.	Cretinism	910	337	73.3	21.7	9.8
M. S.	Cretinism	903	322	74.5	23.1	8.1
C. S.	Cretinism	864	208	68.0	32.6	8.8
Mean values		1,104	353	93.3	27.2	11.0

* When treatment had been instituted before these studies were undertaken, thyroid therapy was discontinued for from four to ten weeks, and blood lipid concentrations were then determined.

patient, with an average of 27.2 per cent. This compares well with the range in normal children. The high degree of correlation between concentration of free cholesterol and total lipids is demonstrated in chart 3 for these children as well as for the normal controls. Although here, too, there is overlapping between the values for normal children and those for children with hypothyroidism, it occurs in the narrow zone represented by the concentrations of 62 to 78 mg. of free cholesterol per hundred cubic centimeters. The determinations for four patients with hypothyroidism fall within this zone. We have thus noted as many children with hypothyroidism in whom there is a normal concentration of free cholesterol in the serum as those in whom there is a normal concentration of total cholesterol.

The level of lipid phosphorus ranged from 8.8 to 13.3 mg. per hundred cubic centimeters, with a mean value of 11.0 mg. per hundred

cubic centimeters. This elevation in concentration over normal follows that of the total lipids fairly closely. In chart 4, in which the values for lipid phosphorus have been plotted against those for total lipids, there is revealed a straight line correlation between them, with little spread. Here, too, there is a considerable zone of overlapping between the lipid phosphorus levels of 8.0 and 10.5 mg. per hundred cubic centimeters in the normal children and in children with hypothyroidism. From a diagnostic standpoint, therefore, the estimation of the level of lipid phosphorus may be considered less useful in this disease than that of total lipids. As is the case in normal children, this value constitutes from 0.9 to 1.3 per cent of that of total lipids.

The effect of treatment with thyroid on concentration of blood lipids is demonstrated in table 4. The concentrations of all the lipid fractions were reduced as a result of therapy to levels which compare closely with those of normal ambulatory children. This is a reversible process, since cessation of treatment for four weeks resulted in most instances in an elevation of the concentration of blood lipids, particularly total lipids, to the previous "untreated level." In some patients, however, it was necessary to withhold therapy for as long as ten weeks before a rise to the previous high levels of total lipids developed.

After treatment, the value for free cholesterol in all but 1 patient was between 21.4 and 29.9 per cent of that for total cholesterol, with an average of 25.1 per cent. This value is similar to that found in untreated patients with hypothyroidism and in normal children.

The relation of the concentration of lipid phosphorus to that of total lipids was not changed by treatment; the value for lipid phosphorus in 95 per cent of the patients remained between 0.9 and 1.3 per cent of that for total lipids.

COMMENT

The concentration of total serum lipids in normal children was found to vary between 363 and 848 mg. per hundred cubic centimeters. As had already been demonstrated, concentrations over 800 mg. per hundred cubic centimeters were uncommon. In 1 patient a concentration of total lipids of 848 mg. per hundred cubic centimeters was found, and in another, 827 mg. per hundred cubic centimeters. There is thus no overlapping in our series between the range of concentrations of total lipids in normal children and that in children with true hypothyroidism.

It has been stated by Boyd [15] that in adults ranging from 15 to 78 years of age there is no relation between increasing age and the concentration of blood lipids. Stoesser [24] concluded that after the third month of life the lipid concentration increases rapidly to approximate

24. Stoesser, A. V.: Altered Lipid Metabolism in Acute Infections of Infants and of Older Children, Am. J. Dis. Child. **56**:1215 (Dec.) 1938.

that of older children. Page [6] observed no determinable effect of age, between 20 and 90 years, on either the amount or the composition of plasma lipids. Offenkranz and Karshan,[19a] on the other hand, found a tendency toward lower values for cholesterol esters in patients under 6 years of age. In our series, there was no constant relation between the age of the patient and the level of any of the blood lipids. The highest

TABLE 4.—*Effect of Treatment on the Concentrations of Blood Lipids in Hypothyroidism*

		Blood Lipid Partition									
		For Untreated Patients *					For Treated Patients				
Patient	Diagnosis	Total Lipids, Mg. per 100 Cc.	Total Cholesterol, Mg. per 100 Cc.	Free Cholesterol, Mg. per 100 Cc.	Percentage Free in Total Cholesterol	Lipid Phosphorus, Mg. per 100 Cc.	Total Lipids, Mg. per 100 Cc.	Total Cholesterol, Mg. per 100 Cc.	Free Cholesterol, Mg. per 100 Cc.	Percentage Free in Total Cholesterol	Lipid Phosphorus, Mg. per 100 Cc.
S. R.	Cretinism.....	1,531	431	136.0	31.5	10.0	541	203	60.7	29.9	4.2
I. S.	Cretinism.....	1,347	433	112.0	25.8	12.2	660	167	60.5	36.0	5.3
A. A.	Cretinism.....	1,342	466	102.0	26.2	10.4	561	174	40.4	23.2	7.0
L. S.	Acquired hypothyroidism....	1,221	445	113.0	25.4	13.8	744	226	54.7	24.2	6.8
A. D.	Cretinism.....	1,198	485	101.5	20.9	11.2					
R. B.	Acquired hypothyroidism....	1,138	211	83.0	39.3	11.8	662	209	58.8	28.1	7.2
P. D.	Acquired hypothyroidism....	1,100	230	62.5	27.2	11.3	670	239	67.6	28.2	6.7
H. N.	Cretinism.....	1,090	353	93.2	26.4	10.0	645	219	47.5	21.6	6.9
B. L.	Cretinism.....	1,053	400	138.0	33.7	12.2	797	243	60.1	24.7	7.6
L. E.	Cretinism.....	1,050	320	82.8	25.9	11.9	408	119	32.2	27.0	5.3
S. C.	Acquired hypothyroidism....	1,034	343	87.5	25.5	11.9	507	170	37.1	21.8	6.1
B. F.	Acquired hypothyroidism....	1,001	269	82.9	30.8	10.9	738	187	50.8	27.1	9.5
W. S.	Cretinism.....	999	400	93.0	23.2	9.4	460	154	33.3	21.6	6.0
A. F.	Cretinism.....	990	337	83.3	24.7	10.0	597	171	37.2	21.7	6.1
D. G.	Cretinism.....	910	337	73.3	21.7	9.8	542	215	46.1	21.4	5.0
M. S.	Cretinism.....	903	322	74.5	23.1	8.1	500	166	36.0	21.7	6.0
C. S.	Cretinism.....	854	208	68.0	32.6	8.8	595	165	38.7	23.4	5.7
Mean values.....		1,104	353	93.3	27.2	11.0	601	189	47.2	25.1	6.3

* When treatment had been instituted before these studies were undertaken, thyroid therapy was discontinued for from four to ten weeks, and blood lipid concentrations were then determined.

concentration of total lipids noted in a normal control was in an infant of 4 months.

From the results of our investigations, it seems evident that estimation of the concentration of total lipids in the serum is of greater value in the diagnosis of hypothyroidism in children than is the determination of cholesterol content alone, since a concentration of cholesterol above the level usually considered normal may occur in apparently normal subjects. On the other hand, in our experience unusual elevations in the concentration of total serum lipids have not been encountered in such

subjects. In untreated patients with unquestioned hypothyroidism, however, there has invariably been noted a decided elevation in concentration of total serum lipids above normal.

In contrast, the concentration of total cholesterol was occasionally found to be within normal limits in patients with severe hypothyroidism. Gildea, Man and Peters [25] considered a cholesterol level below 275 mg. per hundred cubic centimeters sufficiently unusual in hypothyroidism to render the diagnosis in doubt, since such patients were not improved by the administration of thyroid. This view is at variance with our finding of normal cholesterol concentrations in 4 typical cases. These findings are admittedly unusual deviations from the general experience that hypothyroidism is associated with hypercholesteremia. They help to explain the differences in the opinions of various investigators regarding the relation of hypothyroidism to concentration of blood cholesterol. Such variations from the expected cholesterol level may be the result of a constitutional characteristic of the patient which remains constant for him,[26] but they argue against placing too much reliance on the estimation of the cholesterol level in the diagnosis of this disease. Determination of the concentration of total serum lipids may therefore be expected to reveal the occasional instance of hyperlipemia, which would be overlooked if analysis were limited to determining the concentration of serum cholesterol.

The cholesterol concentration in the blood has been considered by Mason, Hunt and Hurxthal [27] a more reliable index of the severity of hypothyroidism than the basal metabolic rate. We have not found any consistent relation between the degree of elevation of the concentrations of either total cholesterol or total lipids and the severity of the disease. Only moderate elevations of the levels of total blood lipids were found in some of our patients with severe hypothyroidism, whereas some of the most marked elevations were encountered in patients with mild acquired hypothyroidism. Thus, it does not follow that mild manifestations of the disease are necessarily associated with but a slight elevation

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25. Gildea, E. F.; Man, E. B., and Peters, J. P.: Serum Lipoids and Proteins in Hypothyroidism, J. Clin. Investigation **18**:739, 1939.

26. (*a*) Turner, K. B., and Steiner, A. J.: A Long Term Study of the Variation of Serum Cholesterol in Man, J. Clin. Investigation **18**:45, 1939. (*b*) Gildea, E. F.; Kahn, E., and Man, E. B.: The Relationship Between Body Build and Serum Lipoids and a Discussion of These Qualities as Pyknophilic and Leptophilic Factors in the Structure of the Personality, Am. J. Psychiat. **92**:1247, 1936. (*c*) Sperry, W. M.: The Concentration of Total Cholesterol in the Blood Stream, J. Biol. Chem. **117**:391, 1937.

27. Mason, R. L.; Hunt, H. M., and Hurxthal, L.: Blood Cholesterol Values in Hyperthyroidism and Hypothyroidism: Their Significance, New England J. Med. **203**:1273, 1930.

of the concentration of blood lipids. These findings therefore suggest the diagnostic value of this determination in borderline hypothyroidism.

The concentration of free cholesterol in our patients with hypothyroidism was from 20.9 to 33.7 per cent of that of total cholesterol. This relation was not altered by treatment with thyroid and agrees well with our findings in normal children. We have thus found the ratio of free to total cholesterol to have no diagnostic bearing in this condition.

A higher degree of correlation has been demonstrated mathematically and graphically between concentrations of total lipids and free cholesterol than between concentrations of total lipids and total cholesterol. However, since normal concentrations of either free or total cholesterol have been noted in our children with hypothyroidism with equal frequency, we have not considered the estimation of free cholesterol to be of greater value in the diagnosis than is the estimation of total cholesterol.

Although the elevation of the level of lipid phosphorus in the serum usually paralleled that of the total lipids, this relation was not constant, so that the concentration of lipid phosphorus alone cannot be used as a diagnostic criterion.

The effect of thyroid therapy on lipid concentration has been described here. All the lipid values which had been markedly elevated in the untreated patient drop to normal after treatment. When therapy is discontinued, these values rise again to levels well above those found in our normal controls. In many patients this occurs within a period of four weeks. In some patients, for reasons as yet unexplained, it is necessary to withhold therapy for a much longer period, even ten to twelve weeks, during which the total lipid concentration rises progressively to the abnormally high "untreated" level. As a rule, in such cases, clinical symptoms reappear early, even though there may be a prolonged delay before the chemical changes in the blood become characteristic. This probably explains the comparatively moderate elevation of the level of total lipids to 854 mg. per hundred cubic centimeters in patient 17. In this patient, the lipid concentration was determined after therapy had been discontinued for only four weeks.

It is of interest, also, that treatment with thyroid for three or four weeks will effect a reduction of the concentration of serum lipids to normal levels in most cases of hypothyroidism. Yet there has occasionally been noted a persistence in the elevation of the level of total lipids for many weeks, in spite of an early clinical response. This may, of course, be due to insufficient treatment. Gildea, Man and Peters [25] noted that none of their patients whose concentration of serum cholesterol was below 316 mg. per hundred cubic centimeters improved under thyroid therapy. We were unable to observe any delay in the response to treatment in any of our 4 patients with normal concentrations of serum cholesterol. Not only was there amelioration of symptoms, but, as can

be seen from table 4, there was a drop in total lipids to normal. Whether these determinations can be relied on as a measure of the adequacy of therapy cannot be stated at the present time. The significance of these determinations can be evaluated only after more extended observations on the response of the level of blood lipids to treatment.

SUMMARY AND CONCLUSIONS

The serum lipid partition of 54 normal children was determined. The normal range is described and discussed.

The serum lipid partition of 17 children with either congenital or acquired hypothyroidism was determined both before and after treatment. There is a decided elevation beyond the normal range of the concentration of total serum lipids in all untreated patients with hypothyroidism.

The concentration of total cholesterol, although elevated in most untreated patients with hypothyroidism, may be within normal limits. The determination of the concentration of total serum lipids is thus demonstrated to be of greater value in the diagnosis of hypothyroidism than is the estimation of total cholesterol.

The concentrations of other serum lipid fractions that were determined are of less diagnostic value in hypothyroidism than the concentration of either total lipids or total cholesterol.

There is no consistent relation between the degree of elevation of the level of total serum lipids in hypothyroidism and the severity of the disease. Mild hypothyroidism may be associated with marked elevations of the level of total lipids. The value of this determination in the diagnosis of borderline hypothyroidism is thus suggested.

Administration of thyroid to patients with hypothyroidism is followed by a reduction in the levels of all the lipid components of the blood to normal. Cessation of treatment is followed by a rise in these values. The time relation between therapy and change in levels of serum lipids is not constant.

The free serum cholesterol constitutes from 19.1 to 30.0 per cent of the total cholesterol content in normal children. An essentially similar relation is found in children with hypothyroidism both before and after treatment.

The concentration of serum lipid phosphorus varies between 0.9 and 1.3 per cent of that of total lipids in normal children. In children with hypothyroidism, both before and after treatment, a similar relation exists.

Case Reports

PAROXYSMAL TACHYCARDIA IN CHILDREN

REPORT OF AN ADDITIONAL CASE

GEORGE D. JOHNSON, M.D.
CHARLESTON, S. C.

It has been suggested that paroxysmal tachycardia in children is more frequent than a search of the literature would indicate. Many adults with this cardiac arrhythmia have stated that the condition dated from childhood.[1] Cases in children have probably been overlooked because of the mildness of symptoms. Taran and Jennings[2] in a review of the literature from 1892 to 1935 found only 52 cases occurring between the ages of 9 days and 15 years. A few of their observations are cited here.

1. Measles and pertussis seem important as causative factors. However, as Shookhoff, Litvak and Matusoff[1] have pointed out, a history of pertussis, though worth noting, may be purely coincidental. 2. Tachycardia is more often auricular than nodal or ventricular, there being in only 3 of the 52 cases a definite diagnosis of the atrioventricular-nodal type. 3. The prognosis seems to depend more on the causative factors than on the type of arrhythmia, though the actual cause has not been determined.

In addition to those recorded by Taran and Jennings,[2] 11 cases have been reported in the literature.[3]

From the Department of Pediatrics, Medical College of the State of South Carolina.

1. Shookhoff, C.; Litvak, A. M., and Matusoff, I.: Paroxysmal Tachycardia in Children: Report of Four Cases and One Postmortem Examination, Am. J. Dis. Child. **43**:93-122 (Jan.) 1932.

2. Taran, L. M., and Jennings, K. G.: Paroxysmal Atrioventricular Nodal Tachycardia in a New-Born Infant, Am. J. Dis. Child. **54**:557-572 (Sept.) 1937.

3. Pereiras, R.: Progressive Paroxysmal Tachycardia in Boy Seven Years Old: Auricular and Nodal Types, Arch. de med. inf. **3**:762-778 (July-Sept.) 1934. Clarke, T. W.: Paroxysmal Tachycardia in Infancy: Case, Arch. Pediat. **52**: 666-675 (Oct.) 1935. Faxen, N.: Paroxysmal Tachycardia and Bundle Branch Block in Boy of Eleven, Acta pædiat. **18**:491-502, 1936. Maarssø, C.: Paroxysmal Tachycardia with Atrioventricular Block in Child Eight Years Old: Case, Hospitalstid. **80**:1140-1143 (Oct. 12) 1937. Kreutzer, R.; Pellerano, J. C., and Schere, S.: Paroxysmal Tachycardia Coexisting with Basedow's Disease in Girl Twelve Years Old, Arch. argent. de pediat. **9**:282-287 (March) 1938. Soeters, J. M.: Paroxysmal Tachycardia in Nursling, Maandschr. v. kindergeneesk. **5**:167-173 (Jan.) 1936. Rubell, I., and Strauss, H.: Fatal Paroxysmal Ventricular

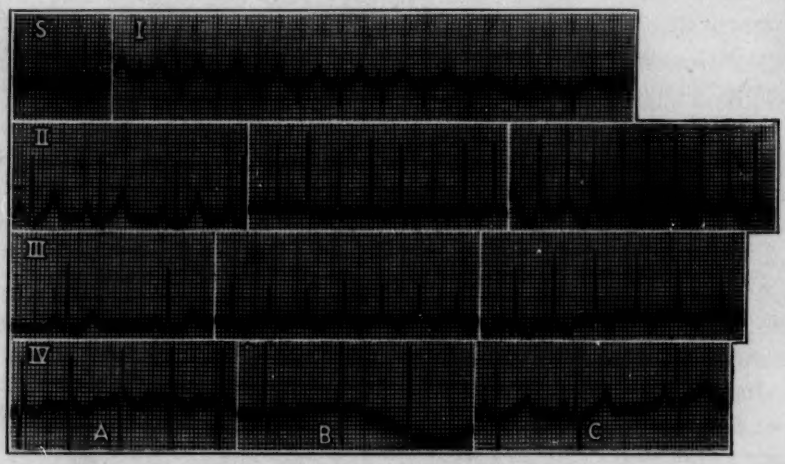
(Footnote continued on next page)

REPORT OF CASE

A. J., a Negro boy born Dec. 17, 1926, had an uneventful infancy. His parents and one brother, born in 1935, were healthy and normal, with no history or evidence of venereal disease, tuberculosis, allergic manifestation or heart disease of any kind.

At 4 years of age, the patient had a severe attack of whooping cough, which, according to the mother, caused the loss of a great deal of blood (probably hemoglobin). He had an attack of "flu" in 1935, but it was not severe. In 1938 he had a severe attack of measles.

Cardiac irregularity was first noticed in 1937, but the exact date was not recalled. The heart would beat rapidly and "'most jump out his chest." This irregularity would start and stop without any apparent cause. Since then, the attacks have come on at any time and may last from a few minutes to an hour or more. There is no pain and no dyspnea of consequence, except during exercise, when difficulty in breathing may be obvious. The paroxysms are more frequent during some weeks than others. On some days attacks are almost continuous.



Electrocardiogram of patient with paroxysmal tachycardia. *S* is a standardization film. *I* is a tracing from lead I; *II* shows tracings from lead II, and *III*, from lead III. In each, *A* shows normal rate; *B* and *C*, rates after exercise. *IV A* (from lead IV) shows normal rate; *IV B* is a tracing from lead IV F, showing normal rate; *IV C* is R wave, showing normal rate. (Interpreted by Drs. J. H. Cannon, James O'Hear and John A. Boone.)

Tachycardia in Young Child, Am. J. Dis. Child. **51**:633-652 (March) 1936. Migliori, V.: Paroxysmal Tachycardia in Child: Case, Bull. d. sc. med., Bologna **108**:185-192 (May-June) 1936. Garzon, W.: Paroxysmal Tachycardia in Girl Two Years Old, Arch. de pediat. d. Uruguay **8**:562-576 (Sept.) 1937. van Buchem, F. S. P., and Keyzer, J. L.: Paroxysmal Tachycardia in Child Three Years Old, Nederl. tijdschr. v. geneesk. **80**:5005-5011 (Nov. 7) 1936. Amberg, S., and Willius, F. A.: Ventricular Tachycardia Occurring in Infant: Cardiac Hypertrophy of Unknown Origin; Postmortem Findings, Proc. Staff Meet., Mayo Clin. **13**:470-474 (July 27) 1938.

Lying down or holding his breath are the only ways he can stop a paroxysm. Pressure on the neck has been tried but seems to have no effect.

He likes to play with other children, but when his heart begins to palpitate he prefers to stop. He is thin, intelligent, friendly and cooperative.

On a number of physical examinations the heart seemed to be regular in rate and rhythm. On the other hand, a rapid rate was found several times. Pulsations of the precordial area were easily seen. Electrocardiographic tracings were obtained during several of these paroxysms. It was impossible to count accurately the pulsations of the radial artery; the fastest rate obtained on the tracing was about 220 per minute. Some rates were about 180 per minute. The other results of the physical examinations were essentially normal. No enlargement of the heart was ever demonstrated clinically. The tonsils were not greatly enlarged.

To date no medication has been advised, because the patient can usually stop the attacks at will. He was advised against riding a bicycle to any great extent or taking any strenuous exercise. At the time he was last heard from he was 12 years of age and in good physical condition except for the occurrence of the abnormal heart rate at irregular intervals.

The accompanying electrocardiogram shows how the heart rate increases during attacks precipitated by exercise.

SUMMARY

An additional case of simple paroxysmal tachycardia in a child is reported. Reference is made to 11 more cases reported since the last comprehensive article on this subject appeared.

PITUITARY DWARFISM WITH ATROPHIC RHINITIS

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AND
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Considerable interest in human dwarfism of the hypophysial type has been stimulated by isolation of the growth hormone. The use of preparations of the anterior lobe of the pituitary containing the growth-promoting principle in children with varyingly subnormal rates of growth has met with indifferent results. Children exhibiting sexual infantilism and defective growth (Lorain-Lévi dwarfs) may be normal at birth and develop adequately until some time in childhood, when growth either ceases or becomes retarded. The arrest involves no special organs and produces a diminutive child whose proportions are normal. The genital retardation is probably not in excess of that of the physical development, but the secondary sexual characteristics are markedly delayed or absent. The mentality may be normal, although the behavior is often immature.

This type of dwarf, as a general rule, is osteologically normal, although the skeletal framework is small. No gross evidence of dystrophy of the bones or joints exists. However, chondroepiphysial changes, poorly outlined centers of ossification with decreased density of the bone, have been described. The centers of ossification usually appear at the normal time, whereas delay in epiphysial closure is found consistently. The basal metabolic rate may be normal; nevertheless, some question exists whether there is coexistent mild hypothyroidism, which may induce slight delay in carpal development and moderate reduction of the basal metabolic rate. In children whose physical development is at variance with the chronologic age basal metabolic rates consistent with the clinical picture are difficult to demonstrate.

The diagnosis of pituitary dwarfism is certain only in those cases in which (1) the hypophysis either has been removed or is known to have been destroyed, necropsy verifying the diagnosis; (2) the roentgenogram

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From the Departments of Pediatrics (Endocrine Clinic) and Otolaryngology, University of Illinois College of Medicine, and the Research and Educational Hospital.

demonstrates the presence of a tumor of the pituitary gland, or (3) definite and continuous response to administration of growth hormone occurs. There is a relative rarity of well marked and clearly recognizable cases of hypophysial insufficiency. Englebach stressed the marked infrequency of defective growth due to either intrasellar or extrasellar tumors. Changes in the size and contour of the sella turcica may be visualized; nevertheless, these changes do not constitute criteria of its function. The assumption of a relation between a small sella turcica or complete bridging of the clinoid processes and statural and sexual maturity is feasible. In view of the rarity of material our patient is of interest.

In addition to dwarfism our patient exhibits atrophic rhinitis. This condition is significant because of the possible relation of the pituitary gland to the nasal mucous membrane, for it is believed that the pituitary gland acts on the mucosa either directly or through the agency of the gonads. Such a relation has been described on a number of occasions, and more recently Mortimer and his associates [1] reported changes in the nasal mucosa of monkeys in response to the administration of estrogenic substances. In this connection, the children of a French-Canadian family consisting of 7 daughters and 2 sons, each with atrophic rhinitis, are interesting. No member of this family has a normal sella; the oldest son is acromegalic; the 2 youngest children are pituitary dwarfs.

REPORT OF A CASE

J. G. (fig. 1) was first seen in November 1936. She was then approximately 12 years old and was definitely retarded in growth. Her parents had given little attention to her growth, since all the members of the family were small, though not markedly stunted. The patient was a full term baby and weighed 5¼ pounds (2,381 Gm.). She was born with two teeth, sat up at 6 months and walked at 18 months of age and apparently continued to develop adequately until she was 8 or 9 years old, when she ceased growing normally. No factors contributing to this status could be determined. She was breast fed until she was 18 months old; though cereals, vegetables and other foods were added earlier, it is questionable whether she received cod liver oil and orange juice.

When originally examined she weighed 46 pounds (20.9 Kg.) and was 45¼ inches (115 cm.) tall—34½ pounds (15.6 Kg.) and 12¼ inches (31 cm.) below the average weight and height for a 12 year old girl.[2] Physical examination revealed little pathologic change other than the nasal disease and a fuller appearance of the left breast. The child was proportioned normally and appeared much

1. Mortimer, H.; Wright, R. P.; Bachman, C., and Collip, J. B.: The Effects of Administration of Estrogenic Hormones on the Nasal Mucosa of the Monkey (Macaca Mulatta), Proc. Soc. Exper. Biol. & Med. **34**:535 (May) 1936. Mortimer, H.; Wright, R. P., and Collip, J. B.: The Effect of Estrogenic Hormones on the Nasal Mucosa, Canad. M. A. J. **35**:615 (Dec.) 1936.

2. Wolf, W.: Endocrinology in Modern Practice, Philadelphia, W. B. Saunders Company, 1936, p. 818, table 5.

younger than her actual age. In July 1937, at the age of 12½, she had an intelligence quotient of 83. In February 1939, at the age of 14, her intelligence quotient was 84. Her schooling and adjustment are discussed elsewhere.[3]

In February 1937, prior to treatment with growth-promoting substance, her nose and sinuses were examined. The nasal septum was fairly straight. There was marked and generalized atrophy of the nasal mucous membrane, visible throughout the nasal passageways. Fetor, crusting and suppuration were evident on the

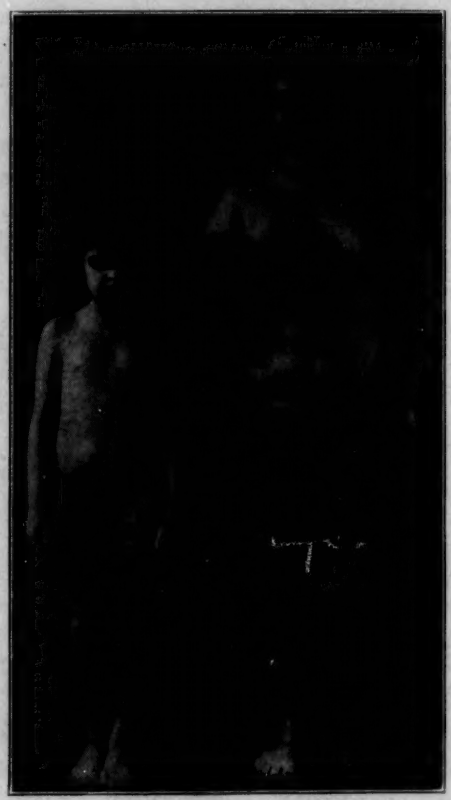

Fig. 1.—J. G. (on left) and obese girl, both 12 years of age.

floor of both sides of the nose. Pharyngitis sicca was present. A number of the teeth were carious. The tonsils had been removed, and the tonsillar fossae were scarred. No postnasal discharge was apparent at this examination. The roentgenogram showed no consistently increased density over any of the paranasal sinuses. After the administration of growth-promoting substance and a little topical treatment, examination on Oct. 6, 1939 revealed crusting in the posterior portion of the right side of the nose. Although in general the nose appeared cleaner and the mucosa pink and glistening, fetor was still noticeable. The generalized atrophy was as prominent as before treatment.

3. Foster, R.; Brown, A. W., and Bronstein, I. P.: The Mental Development of a Group of Dwarfish Children, Proc. Am. A. Ment. Deficiency **44**:143, 1939.

Roentgenograms of the skull in the lateral direction (fig. 2), made at the time of the first visit and subsequently, revealed that the sella turcica was slightly larger than usual and contained a roughly circular deposit of calcium. Films of both wrists in the posteroanterior direction showed general underdevelopment and but seven carpal bones; a similar series of films taken one and a half years later showed that retardation was still present. The initial roentgenogram of the right leg displayed an irregular area of rarefaction in the upper end of the right tibia. There were similar findings [4] in subsequent films.

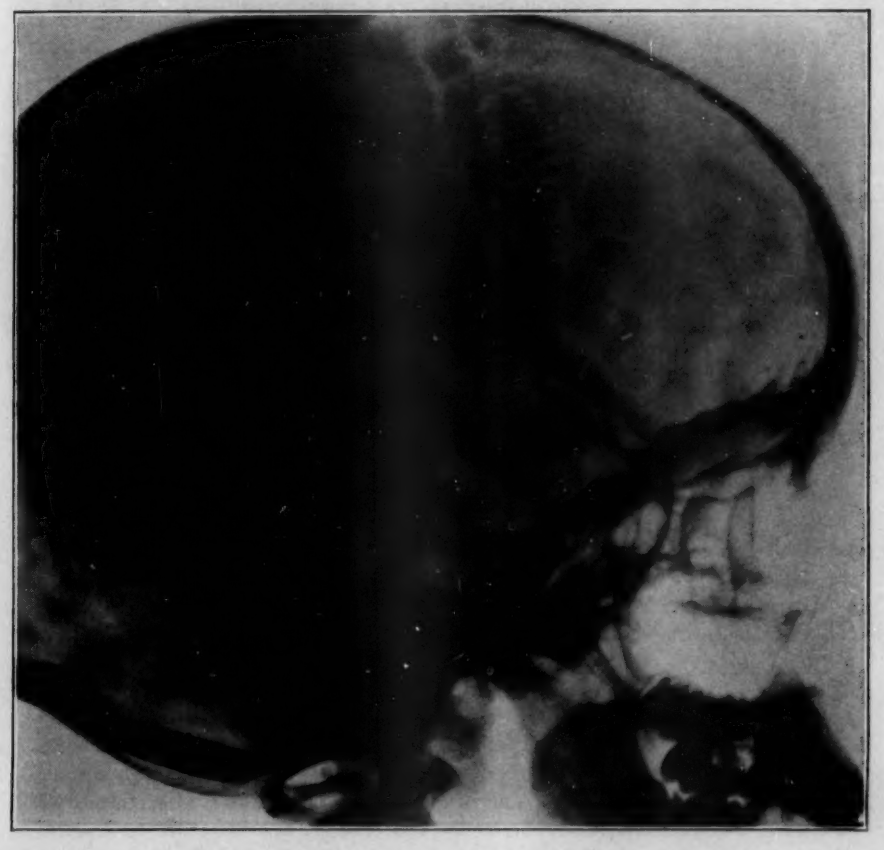

Fig. 2.—Roentgenogram of the skull, showing slightly enlarged sella turcica and the circular deposit of calcium within it.

Examination of the ocular fundi and the visual fields revealed essentially a normal condition. The blood pressure was 100 systolic and 80 diastolic. The Kahn serologic reaction was negative. Examinations of the urine before and after the administration of growth-promoting substances gave normal results. The original blood count showed a hemoglobin content of 70 to 75 per cent; 3,900,000 erythrocytes, and 9,150 leukocytes, with 76 per cent lymphocytes and 24 per cent

4. This finding is worthy of some speculation. It may have been a developmental variation, although the question arises whether it was remotely related to the pituitary involvement.

neutrophils. A second blood count revealed a hemoglobin content of 80 per cent; 3,900,000 erythrocytes, and 11,300 leukocytes, with 47 per cent lymphocytes, 52 per cent neutrophils and 1 mononuclear. The serum calcium was 9.7 mg. per hundred cubic centimeters of blood; the serum phosphorus, 5.5 mg., and the blood phosphatase, 8.6 Bodansky units.

In determining the basal metabolic rate, standards [5] both of calories for weight and calories for height were used. The results of the studies were as follows:

	Calories per Hour		Basal Metabolic Rate	
	Initial Visit	1½ Yr. Later	Initial Visit	1½ Yr. Later
Value determined by test.....	38.6	41.6		
Normal value based on weight.	36	51.1	+7	−19
Normal value based on height..	35.3	37.3	+9	+11

The dextrose tolerance test revealed the following values:

	Blood Sugar, Mg. per 100 Cc.	Urinary Sugar
Fasting	87	
After ingestion of dextrose		
½ hour	118	All
1 hour	97	Negative
1½ hours	90	
2 hours	83	
3 hours	68	

Therapy was given over a period of thirty-one months; in all the child received 186.5 cc. of growth-promoting substance. The parents were uncooperative, and at best the treatment was so irregular that occasionally months elapsed without therapy. At the conclusion of treatment both breasts seemed a little fuller; otherwise no secondary sexual characteristics had appeared. The total gain in weight from the beginning of treatment was 14¼ pounds (6.5 Kg.), and the increase in height 3¼ inches (8.3 cm.). The growth-promoting substances were administered intramuscularly, and three different products were used. One of these was presumably a pure growth-promoting substance with no extraneous materials. A second contained some gonad-stimulating material, thyrotropic substance and prolactin. The last material used was a growth-promoting complex free from gonadotropic and thyrotropic substances but containing appreciable amounts of adrenotropic and lactogenic factors. The assayed potency was 100 growth units per cubic centimeter, and was standardized by the effect on the growth of recently hypophysectomized but otherwise untreated rats. While treatment with preparations of the anterior lobe of the pituitary is substitution therapy insofar as involvement of the pituitary gland itself is concerned, nevertheless through such stimulation effects from the action of thyroid, gonads and adrenal glands may be produced.

COMMENT

Our case is that of Lorain-Lévi dwarf with the infrequent feature of a calcified mass within the sella turcica. The girl presumably had

5. Talbot, F. B.; Wilson, C. B., and Worcester, J.: Basal Metabolism of Girls: Physiologic Background and Application of Standards, Am. J. Dis. Child. **53**:273 (Jan., pt. 2) 1937.

a lesion of the hypophysis which became calcified and whcih obviously interfered seriously with the growth and sexual functions. Symptoms of intracranial hypertension did not exist. There was no vomiting, disturbance of gait, headache or disorientation, and the ocular fundi and visual fields were normal.

The concomitant atrophic rhinitis adds further interest to this case. Recently Eagle and his associates [6] employed estrogenic substances in treating a series of patients with atrophic rhinitis. Effects of androgen on the nasal mucosa of both human subjects and monkeys have also been studied.[7] In Eagle's series specimens were taken for biopsy from the diseased middle turbinate bone of 14 patients before, during or after treatment. Microscopic studies of the specimens failed to reveal obvious or definite changes in a single direction. The experience of these investigators substantially corroborates the position taken by one of us [8] elsewhere questioning the value of a single biopsy for the purpose of obtaining sufficient information about the entire nasal mucosa.

We did not employ estrogens because of the possibility of producing premature epiphysial closure, thereby interfering with growth, which we most desired in our patient. Definite proof is still wanting as to the untoward effects of estrogen, testosterone and excessive amounts of gonadotropic material on preadolescent children, particularly in closing the epiphyses too early.[9] The possibility of such effects, nevertheless, must be kept in mind and caution exercised in the use of these products. Since there is considerable evidence that growth hormones and gonadotropic hormones are antagonistic, growth-promoting substance should be free from the gonadotropic principle.

The prolonged administration of growth-promoting materials apparently does not interfere with the onset of puberty, or with the spurt of growth that may occur in this period, but it is not without some undesirable effects, as, for instance, glycosuria. Glycosuria was not present in our patient after the total amount of growth hormone was administered. Thyroid therapy was not instituted, although the administration of thyroid enhances the action of the growth hormone.[10]

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6. Eagle, W. W.; Baker, R. D., and Hamblen, E. C.: Atrophic Rhinitis: Treatment with Estrogenic Substances, with Biopsy Before and After Treatment, Arch. Otolaryng. **30**:319 (Sept.) 1939.

7. Tebbutt, H. K.: Male Hormone: Effect upon Nasal Mucosa of Man and Monkey, New York State J. Med. **38**:332 (March 1) 1938.

8. Fabricant, N. D.: The Nasal Biopsy: A Critique of Current Methods, Laryngoscope, to be published.

9. Untoward Effects from Gonadotropic Substance, Queries and Minor Notes, J. A. M. A. **113**:1884 (Nov. 25) 1939. Bronstein, I. P.: Unpublished data.

10. Smith, P. E.: Increased Skeletal Effects in A. P. Growth-Hormone Injections by Administration of Thyroid in Hypophysectomized, Thyro-Parathyroidectomized Rats, Proc. Soc. Exper. Biol. & Med. **30**:1252 (June) 1933.

SUMMARY

The case of a pituitary dwarf with sexual infantilism (Lorain-Lévi type), exhibiting two unusual features, a calcified lesion in the sella turcica and atrophic rhinitis, is described. Rarefaction of the tibia was noted.

Estrogens, which have been employed by others in treatment of atrophic rhinitis, were not used with our patient because of the possibility of premature epiphysial closure.

The irregular administration of growth-promoting substances over a period of approximately two and one-half years was presumably responsible for a gain in weight and an increase in height but had no apparent effect on the atrophic rhinitis.

1819 West Polk Street.

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HEREDOFAMILIAL DEVIATIONS

II. ENLARGED PARIETAL FORAMENS COMBINED WITH OBESITY, HYPOGENITALISM, MICROPHTHALMOS AND MENTAL RETARDATION

JOSEF WARKANY, M.D.
AND
THOMAS S. WEAVER, M.D.
CINCINNATI

J. L. R., a Negro boy aged 11½ years, was admitted to the endocrine clinic of the Children's Hospital because of obesity and cryptorchidism. There were several unusual findings on physical examination which appear to justify the presentation of this case.

REPORT OF A CASE

Past History.—The patient had been delivered normally at term and appeared to be well after birth. No record of his birth weight was available. He had been breast fed for two or three months and had received cod liver oil irregularly. His first teeth appeared at 1 year of age, and he walked at 3 years. Of the diseases of childhood he had only had pertussis. Between the ages of 6 months and 2 years he had a series of four or five generalized convulsions, which in each instance lasted only a few minutes. There was a history of occasional infections of the respiratory tract and of purulent otitis media on one occasion. There were no abnormal gastroenteric symptoms other than a tendency to constipation. The patient voided frequently during the day and usually once during the night. At the time of examination, he was still in the first grade of school, where he had been enrolled three years previously.

Family History.—The mother, aged 28, was mentally retarded. Her general health had been good in spite of a small goiter, which had been present for several years. The Wassermann reaction of her blood was said to have been negative in 1938. The details of the father's health were not known, but he was apparently well when last heard from. The patient was the result of the only pregnancy of his mother. Unfortunately, a detailed family history could not be obtained because of the mother's poor memory. The only related abnormality ascertained was the occurrence of polydactylism in one of the mother's brothers.

Examination.—The patient (fig. 1) was found to be 12 cm. below the average height for his age and about 10 Kg. overweight for his height. His weight was 36.5 Kg. His dimensions were as follows: height, 128 cm.; upper measurement, 58 cm; lower measurement, 70 cm.; span, 137 cm.; circumference of head, 50.5 cm.; circumference of chest, 72 cm.; abdominal circumference, 74 cm. Scars were present on the forehead and upper lip. The distribution of fat was of the adiposogenital type, with a thick panniculus in the mammary and abdominal regions.

The appearance of the skull, which was definitely small in diameter (50.5 cm., as compared with 53 cm. for the average value), was suggestive of "tower head." There was ptosis of the left lid, and the left palpebral fissure appeared smaller than the right. With the left eye at rest, there was an inward deviation of approximately 40 degrees, and transient nystagmus was noted. The external ocular movements were otherwise normal. The left cornea was small and cloudy; the pupils reacted normally, and the left fundus could not be seen. The right eye, including the fundus, and the ear drums appeared normal. The tongue was large, and the teeth were in poor condition. The hard palate formed a high Gothic

Fig. 1.—Photograph showing obesity in the mammary and abdominal regions, tower head, ptosis of the left eyelid and genu valgum.

arch, the uvula and soft palate appearing normal. The sternum was depressed. Examination of the heart, lungs and abdomen showed nothing abnormal. The testes were undescended, and the penis was small. The joints of the elbows and fingers were overextensible, and genu valgum was present. The thumbs were spadelike, and the little fingers incurved at the terminal phalanx. The reflexes were normal. His intelligence quotient was 38.

Laboratory Findings.—Examination of the urine and blood revealed nothing abnormal. The Kahn reaction of the blood was negative. The tuberculin test

with purified protein derivative no. 1 was negative. The basal metabolic rate was —16 per cent. The details of the dextrose tolerance test were as follows:

	Blood Sugar, Mg. per 100 Cc.	Urinary Sugar
Fasting	90	0
After ingestion of dextrose		
½ hour	224	+
1 hour	185	+++
2 hours	156	+
3 hours	72	Trace

Fig. 2.—Roentgenograms of the skull showing large parietal foramens.

On a high carbohydrate diet sugar (+) was noted in the urine on several occasions. We believe that this boy has an abnormality of carbohydrate metabolism; a latent diabetic or prediabetic state may be suspected.

Roentgenograms of the skull showed a fairly round area about the size of a trephine opening in the posterior and lower portion of each parietal bone. A narrow longitudinal osseous defect was present in the midline (fig. 2). The remainder of the skull appeared normal. Roentgenograms of the wrists and left elbow showed evidence of delayed ossification. Roentgenograms of the chest showed nothing abnormal; and the spine, pelvis, hips and intervertebral disks also appeared normal. After the roentgenograms had been examined a small depressed area could be palpated in the lower portion of each parietal bone. Roentgenograms of the skull of the patient's mother showed no evidence of osseous disease.

Summary.—The most prominent abnormalities were obesity, a disturbance of carbohydrate metabolism, hypogenitalism, microphthalmos and cloudy cornea of the left eye, enlarged parietal foramens and mental retardation.

COMMENT

Obesity, hypogenitalism and mental retardation are frequently found in association in patients requiring study from the point of view of endocrine dysfunction, and these symptoms may be accompanied by other developmental defects. When retinitis pigmentosa and polydactylism or syndactylism are also present, the condition has been termed the "Laurence-Moon-Biedl syndrome." Ocular defects other than retinitis pigmentosa have been found in similar cases. A combination with coloboma of the iris has been called Biemond's syndrome.[1] Optic atrophy as one of the associated symptoms has been frequently observed.[2] Cavallacci's cases of microphthalmos and the diencephalohypophysial syndrome [3] resemble our case to a certain extent. Polydactylism was not present in our patient, but a maternal uncle was said to have six fingers.

The boy whose case is presented in this report had a skeletal developmental defect, namely enlarged parietal foramens, which deserves special mention. Enlarged parietal foramens have been known to anatomists since the eighteenth century.[4] However, the anomaly appears to be rare, and Pamperl,[5] in 1919, was able to find reports of only 36 cases

1. van Bogaert, L., and Delhaye, A.: Observation d'un syndrome familial nouveau (Biemond) proche de la maladie de Laurence-Moon-Bardet, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:683-691 (May 11) 1936.

2. Reilly, W. A., and Lisser, H.: Laurence-Moon-Biedl Syndrome, Endocrinology **16**:337-357 (July-Aug.) 1932.

3. Cavallacci, G.: Sindromi ipofiso-diencefaliche con microftalmo congenito. Ipotesi sulla loro patogenesi e considerazioni su possibili rapporti con le sindromi tipo Laurence-Biedl ed affini, Arch. di ottal. **44**:1-64 (Jan.) 1937.

4. Lancisi, J. M.: De subitaneis mortibus, Rome, J. F. Buagni, 1707, p. 178. Lobstein, J. F.: De nervis durae matris (1772), in Scriptores neurologici minores selecti, Leipzig, J. F. Junius, 1791, vol. 1, pp. 89-107; cited by Pamperl.[5]

5. Pamperl, R.: Foramina parietalia permagna, Deutsche Ztschr. f. Chir. **148**:91-110 (Jan.) 1919.

in the literature. If a second case of Greig [6] and the cases of Virchow [7] are added, only 41 instances had been reported up to as late as 1919. Since that time this number has increased rapidly, perhaps because roentgenologic examination of the skull is more frequently employed. In the majority of older reports, the diagnosis was not made during life, and little information was given about other somatic abnormalities of patients with this defect. Now that roentgenologic examination reveals enlarged parietal foramens in living persons, studies of the patient as well as of his relatives are usually possible without much difficulty. Certain interesting facts can be learned from these investigations.

The occurrence of enlarged parietal foramens is frequently familial.[8] In some families only 2 members among a larger number are affected, while in others there may be a high incidence of the defect. Thus, in five generations of the Catlin family, as described by Goldsmith,[8c] 16 of the 56 members examined showed the anomaly.

The statement has been made that as a rule enlarged parietal foramens are found in persons or families otherwise perfectly normal. A review of the literature fails to confirm this statement. Various abnormalities of the skull, including microcephalus,[9] hydrocephalus,[10]

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6. Greig, D. M.: (*a*) Two Cases of Congenital Symmetrical Perforation of the Parietal Bones, Edinburgh M. J. **18**:205-209 (March) 1917; (*b*) Abnormally Large Foramina Parietalia, ibid. **34**:629-648 (Nov.) 1927.

7. Virchow, R.: Colossale Foramina parietalia an menschlichen Schädeln, Verhandl. d. Berl. Gesellsch. f. Anthrop., 1896, pp. 593-599.

8. (*a*) Greig, D. M.: Congenital and Symmetrical Perforation of Both Parietal Bones, J. Anat. & Physiol. **26**:187-191, 1891-1892. (*b*) Symmers, W. St. C.: A Skull with Enormous Parietal Foramina, ibid. **29**:329, 1894-1895. (*c*) Goldsmith, W. M.: The Catlin Mark: The Inheritance of an Unusual Opening in the Parietal Bones, J. Heredity **13**:69-71, 1922. (*d*) Neurath, R.: Ueber hereditäre Ossifications-Defekte der Scheitelbeine (Foramina parietalia permagna hereditaria), Ztschr. f. Kinderh. **32**:121-128, 1922. (*e*) Cohn, M.: Die vererbbaren Verknöcherungsdefekte der Scheitelbeine, Med. Klin. **20**:857-860 (June 22) 1924. (*f*) Lelong, M., and Bosquet: Lacunes congénitales de la voûte, crânienne chez un enfant de 5 ans; caractère familial, Bull. Soc. de pédiat. de Paris **30**:161-165, 1932. (*g*) Weber, F. P., and Schwarz, E.: Hereditary Large Parietal Foramina, Proc. Roy. Soc. Med. **29**:122-125 (Dec.) 1935. (*h*) Pepper, O. H. P., and Pendergrass, E. P.: Hereditary Occurrence of Enlarged Parietal Foramina: Their Diagnostic Importance, Am. J. Roentgenol. **35**:1-8 (Jan.) 1936. (*i*) Hässler, E.: Fenestrae Parietales Symmetricae, Monatschr. f. Kinderh. **64**:337-340, 1936. (*j*) Irvine, E. D., and Taylor, F. W.: Hereditary and Congenital Large Parietal Foramina, Brit. J. Radiol. **9**:456-462 (July) 1936. (*k*) Alley, R. G.: Enlarged Parietal Foramina: Report of Additional Family Showing This Anomaly, Radiology **27**:233-235 (Aug.) 1936. (*l*) Voigt, R.: Ueber die "Fenestrae parietales symmetricae," Monatschr. f. Kinderh. **70**:224-231, 1937. (*m*) Travers, J. T., and Wormley, L. C.: Enlarged Parietal Foramina, Am. J. Roentgenol. **40**:571-579 (Oct.) 1938.

9. (*a*) Turner, W.: On Some Congenital Deformities of the Human Cranium, Edinburgh M. J. **11**:7 and 133, 1865. (*b*) Wraný: Abnorm Weite der Foramina

(Footnotes continued on next page)

tower head and asymmetry,[11] have been described in association with large parietal foramens. Abnormalities of the spinal column, funnel chest, coxa valga, syndactylism, polydactylism and supernumerary epiphyses[12] have been observed in persons with enlarged parietal foramens. A combination with congenital heart disease was seen in 1 of Neurath's patients,[8d] and harelip was present in a case reported by Irvine and Taylor.[8j] In Hässler's case the patient's maternal uncle had harelip.[8l] Ptosis of the eyelid was present in our case, as well as in Zarfl's.[9f] Exophthalmos,[12] microphthalmos, cloudy cornea (our case), nystagmus, strabismus (Pamperl[5] and our case), partial[8d] or complete[9e] optic atrophy, choked disk,[9f] absence of an auricle and atresia of the external auditory canal[13] may accompany enlarged parietal foramens. Deaf-mutism was present in 1 of Neurath's patients[8d] and in a brother of a patient of Travers and Wormley.[8m] Endocrine anomalies in such patients are of particular interest. Retardation of growth, ossification and dentition are mentioned by Zarfl[9f] and dwarfism by Bourneville and Paul-Boncour.[9e] Obesity (Bourneville and Paul-Boncour[9e] and our case), as well as cryptorchidism (Neurath,[8d] Zarfl[9f] and our case), may occasionally be found. Enlarged parietal foramens have been observed in cases of mental retardation[9e, f] and in a case of mongolism.[6b] Headaches,[14] choreiform movements[5] and epilepsy[15] occur as neurologic complications.

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parietalia, Vrtljschr. f. prakt. Heilk. **89**:108, 1866; cited by Greig.[6b] (*c*) Broca, P.: Sur la perforation congénitale et symmétrique de deux pariétaux, Bull. Soc. d'anthropol. de Paris **10**:192-199, 1875. (*d*) Paterson, A. M., and Lovegrove, F. T.: Symmetrical Perforations of the Parietal Bones: Including an Account of a Perforated and Distorted Cranium from the Liverpool Museum, J. Anat. & Physiol. **34**:228-237, 1900. (*e*) Bourneville, and Paul-Boncour, G.: Considérations sur la morphologie crânienne dans ses rapports avec l'état pathologique du cerveau, Bull. et mém. Soc. d'anthropol. de Paris **2**:35-46, 1902. (*f*) Zarfl, M.: Fenestrae parietales symmetricae, Ztschr. f. Kinderh. **57**:54-66, 1934.

10. Simon, T.: (*a*) Ein Fall von abnormer Erweiterung der Foramina parietalia, Virchows Arch. f. path. Anat. **51**:137-139, 1870; (*b*) Ein neuer Fall abnorm weiter Foramina parietalia, ibid. **55**:536, 1872.

11. Gruber, W.: Ueber congenital abnorm weite Foramina parietalia, Virchows Arch. f. path. Anat. **50**:124-134, 1870; Ueber einem neuen Fall eines congenital abnorm weiten Foramen parietale mit Bemerkungen über die zur Ermittelung der Ursache seines Auftretens aufgestellten Hypothesen und anderen Erörterungen, ibid. **68**:305-324, 1876.

12. Neurath.[8d] Zarfl.[9f]

13. Eckhardt, H.: Knochendefekt im rechten Os parietale bei einem Kinde, Arch. f. Kinderh. **67**:444-453, 1919.

14. Irvine and Taylor.[8j] Voigt.[8l] Travers and Wormley.[8m] Bourneville and Paul-Boncour.[9e] Zarfl.[9f]

15. Reitsema, J. M.: A Congenital Case of Abnormally Large Parietal Foramina, Psychiat. en neurol. bl. **6**:309-311, 1902. di Gaspero, H.: Zur Kenntnis der abnorm grossen Foramina parietalia, Mitt. d. Ver. d. Aerzte in Steiermark **48**:355-362, 1911. Pamperl.[5] Bourneville and Paul-Boncour.[9e]

These examples may suffice to indicate how frequently morphologic and functional abnormalities are seen combined with enlarged parietal foramens.

A number of developmental abnormalities were present in our patient, but it is not intended to use them to establish a new "syndrome." One could consider the case as representing another "atypical" form of the Laurence-Moon-Biedl syndrome. It has been pointed out, however, that even this syndrome can hardly be considered a disease entity, since incomplete or transitional forms are more numerous than the typical ones.[16] The case presented here is merely one of another combination of developmental abnormalities, a combination which is probably rather rare, since one of its elements, enlarged parietal foramens, is not frequently encountered.

A variety of etiologically different conditions may resemble enlarged parietal foramens in the roentgenogram. Defects in the bones of the skull are seen in association with meningoencephalocele, syphilis, xanthomatosis (Schüller-Christian syndrome), multiple myeloma, multiple malignant metastases, renal and celiac rickets, cleidocranial dysostosis and after trauma or openings made for ventriculographic examination. If one bears in mind the possible occurrence of enlarged parietal foramens, usually symmetrically placed on each side of the posterior third of the sagittal suture and irregularly shaped, with well defined margins, the diagnosis is relatively easily made.

In certain rare cases the differential diagnosis may offer difficulties. For instance, unilateral enlargement of one parietal foramen may resemble a traumatic, metastatic or xanthomatous lesion. Diagnosis of the condition in a newly born infant is sometimes difficult, owing to the fact that a single large defect may extend across the sagittal suture and into both parietal bones. This is the forerunner of enlarged parietal foramens,[9f] since by growth of the parietal bones and the union of two sagittal osseous processes the final openings are formed. In meningocele or encephalocele the defect of the skull is covered by a tumor and osseous defects connected with them are usually seen in the occipital bone or in the anterior or middle portion of the base of the skull [17] and not in the parietal bones. In cleidocranial dysostosis large, nonossified areas and open sutures and fontanels may be seen, but this condition can be confused with enlarged parietal foramens in young infants only; in older children there is no resemblance to parietal foramens. The maplike

16. (*a*) Warkany, J.; Frauenberger, G. S., and Mitchell, A. G.: Heredofamilial Deviations: I. The Laurence-Moon-Biedl Syndrome, Am. J. Dis. Child. **53**:455-470 (Feb.) 1937. (*b*) Hecker, A. O., and Warren, V. C.: Girdle Type Adiposity Among Mentally Deficient Males, ibid. **54**:1257-1271 (Dec.) 1937.

17. Brailsford, J. F.: Radiology of Bones and Joints, Baltimore, William Wood & Company, 1934.

skull of the Schüller-Christian syndrome, or xanthomatosis, will be easily recognized if exophthalmos and diabetes insipidus are also present, which is not always the case. Obesity, hypogenitalism, dwarfism, exophthalmos, ptosis and choked disk have been described in cases of xanthomatosis,[18] as well as in combination with enlarged parietal foramens. A multiplicity of lesions in the skull which increase in size is usually indicative of xanthomatosis.

Multiple lesions of the skull are also seen in cases of myeloma and of metastases of malignant tumors; they are differentiated from enlarged parietal foramens by their irregular position and varying shape and size. Areas of decalcification, sometimes well defined, may be seen in the skulls of children who have renal or celiac rickets. In such cases all the bones of the skull are affected. Syphilitic lesions have no typical location and are recognized by their association with positive serologic reactions. Traumatic defects in the parietal region may simulate enlarged parietal foramens and make the differential diagnosis rather difficult, but the presence of other developmental anomalies [12] or a reliable history is of aid in recognizing the cause of the defect.

Openings made for ventriculographic examination are usually farther from the midline than enlarged parietal foramens, and they are round, of equal size and symmetric.[8m]

SUMMARY

Enlarged parietal foramens combined with obesity, disturbance of carbohydrate metabolism, hypogenitalism, microphthalmos and mental retardation are described in a Negro boy 11½ years of age. These abnormalities are considered as coordinated developmental defects. It is pointed out that some of these defects are present in the Laurence-Moon-Biedl syndrome, while others have not been seen in this combination.

A review of the literature reveals that enlarged parietal foramens occur frequently in children who have other developmental abnormalities.

The differential diagnosis of enlarged parietal foramens and other defects of the skull is discussed.

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18. Atkinson, F. R. B.: Schüller-Christian's Disease, Brit. J. Child. Dis. **34**: 28-47 (Jan.-March) 1937.

Progress in Pediatrics

EQUINE ENCEPHALOMYELITIS IN INFANCY

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Knowledge of the greater susceptibility of young laboratory animals to infection with the eastern and western strains of equine encephalomyelitic virus, together with the fact that the majority of cases of equine encephalomyelitis in human beings have occurred in children,[1] renders this disease particularly worthy of consideration by pediatricians in the differential diagnosis of febrile disorders associated with encephalitic manifestations. The necessity for such differentiation is especially obvious during the summer and fall months in those areas where encephalomyelitis has been known to occur among horses. Few observations on the postencephalitic state in human beings after infection with these viruses have been recorded. However, recently several reports have appeared in the literature [2] which bear out Feemster's earlier prediction [3] that certain patients with this disease would have paralyses, mental changes and other permanent residuals. After a brief review of the literature, the clinical and serologic observations in the case of an infant who was infected with the western strain of the virus during the first month of his life will be described in the present paper.

It had been suspected for some time that both eastern and western strains of the virus could produce a serious and highly fatal disease in human beings.[4] Since the autumn of 1938, the virus has been recovered

From the Department of Pediatrics of the University of Minnesota Medical School.

1. Sabin, A. B., and Olitsky, P. K.: Age of Host and Capacity of Equine Encephalitis Viruses to Invade the CNS, Proc. Soc. Exper. Biol. & Med. **38**:595 (May) 1938. Olitsky, P. K.: Equine Encephalomyelitis, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 4, chap. 7, p. 35.

2. Farber, S.; Hill, A.; Connerly, M. L., and Dingle, J. H.: Encephalitis in Infants and Children Caused by the Virus of the Eastern Variety of Equine Encephalitis, J. A. M. A. **114**:1725 (May 4) 1940. David, J. H.: Equine Encephalomyelitis (Western Type) in Children, J. Pediat. **16**:591 (May) 1940.

3. Feemster, R. F.: Outbreak of Encephalitis in Man Due to the Eastern Virus of Equine Encephalomyelitis, Am. J. Pub. Health **28**:1403 (Dec.) 1938.

4. Meyer, K. F.; Haring, C. M., and Howitt, B. F.: The Etiology of Epizoötic Encephalomyelitis of Horses in the San Joaquin Valley, 1930, Science **74**:227

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from a number of patients dying of the disease.[5] As clinical manifestations alone are inadequate for differentiation of equine encephalomyelitis from other types of acute encephalitis, specific diagnosis depends on the recovery of the virus either from the serum of the patient in the early acute stages of the disease or from the brain in fatal cases or on the demonstration of a significant titer of protective antibodies for the virus in the serum during convalescence. It has been shown that a virus originally secured by Fothergill from the brain of a child would reproduce the typical form of the disease in a nonimmune horse [6] and that this one strain, at least, is indistinguishable from the eastern type of equine encephalomyelitis virus.

Both strains of the virus have been recovered from widely scattered sources, the Appalachian Mountains apparently forming a rough geographic dividing line between the eastern and the western types. Although there is a similarity in the clinical picture of the disease produced experimentally by the two strains (except for a more fulminating course when the infection is caused by the eastern strain), they have been shown to be immunologically distinct. The characteristics of these viruses, along with the pathologic changes they produce, have been intensively studied.[7] In 1933, Ten Broeck and Merrill [7a] stated: "It is

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(Aug. 28) 1931. Meyer, K. F.: A Summary of Recent Studies in Equine Encephalomyelitis, Ann. Int. Med. **6**:645 (Nov.) 1932; Equine Encephalomyelitis, North Am. Vet. **14**:30 (June) 1933. Reimann, H. A.: Infectious Diseases: Review for 1938, Arch. Int. Med. **64**:386 (Aug.) 1939. Fothergill, C. D.: Equine Encephalomyelitis, Virus and Rickettsial Diseases, in Harvard School of Public Health Symposium, Cambridge, Mass., Harvard University Press, 1940, pp. 661-683.

5. Fothergill, L. D.; Dingle, J. H.; Farber, S., and Connerly, M. L.: Human Encephalitis Caused by the Virus of the Eastern Variety of Equine Encephalomyelitis, New England J. Med. **219**:411 (Sept. 22) 1938. Webster, L. T., and Wright, F. H.: Recovery of Eastern Equine Encephalomyelitis from Brain Tissue of Human Cases of Encephalitis in Massachusetts, Science **88**:305 (Sept. 30) 1938. Wesselhoeft, C.; Smith, E. C., and Branch, C. F.: Human Encephalitis: Eight Cases with Four Due to the Virus of Equine Encephalomyelitis, J. A. M. A. **111**:1735 (Nov. 5) 1938. Howitt, B. F.: Recovery of the Virus of Equine Encephalomyelitis from the Brain of a Child, Science **88**:445 (Nov. 11) 1938; Recovery of the Virus of Equine Encephalomyelitis (Western Type) from Human Blood Serum, ibid. **88**:541 (June 9) 1939.

6. Schoening, H. W.; Giltner, L. T., and Shahan, M. S.: Equine Encephalomyelitis Produced by Inoculation of Human Encephalitis Virus, Science **88**:409 (Oct. 28) 1938.

7. (*a*) Ten Broeck, C., and Merrill, M. H.: A Serological Difference Between Eastern and Western Equine Encephalomyelitis, Proc. Soc. Exper. Biol. & Med. **31**:217 (Nov.) 1933. (*b*) Bauer, J. H.; Cox, H. R., and Olitsky, P. K.: Ultrafiltration of the Virus of Equine Encephalomyelitis, ibid. **33**:378 (Dec.) 1935. (*c*) Lazarus, A. S., and Howitt, B. F.: Ultrafiltration of Virus of Equine Encephalomyelitis (Russian Strain, Moscow no. 2), ibid. **36**:595 (June) 1937. (*d*)

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apparent that the western strains are serologically identical, and that the eastern strains differ from them but not from each other." They were able to demonstrate the presence of neutralizing antibodies in the serums of 4 horses which had evidently recovered from an infection with the western strains. By means of filtration experiments, Bauer, Cox and Olitsky [7b] showed that both strains of the virus would pass through a collodion membrane with an average pore diameter of 66 millimicrons but not through one with a 60 millimicron diameter, indicating that they have the same filtration end point and consequently the same particle size as the virus of St. Louis encephalitis, approximately 20 to 30 millimicrons as previously measured by Bauer, Fite and Webster. This work was later partially confirmed by Lazarus and Howitt,[7c] who used strains of virus isolated in New Jersey and California. Using the

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Wyckoff, R. W. G.: Ultracentrifugal Concentration of a Homogeneous Heavy Component from Tissues Diseased with Equine Encephalomyelitis, ibid. **36**:771 (June) 1937. (*e*) Howitt, B. F.: Method of Transmission of Immunity to Equine Encephalomyelitis in the Guinea Pig, J. Infect. Dis. **61**:88 (July-Aug.) 1937. (*f*) Hurst, E. W.: Infection of the Rhesus Monkey and Guinea Pig with the Virus of Equine Encephalomyelitis, J. Path. & Bact. **42**:271 (Jan.) 1936. (*g*) Howitt, B. F.: The Moscow no. 2 Strain of Equine Encephalomyelitic Virus as Compared with Other Strains of Equine Encephalomyelitic Viruses, J. Infect. Dis. **63**:269 (Nov.-Dec.) 1938. (*h*) Beck, C. E., and Wyckoff, R. W. G.: Venezuelan Equine Encephalomyelitis, Science **88**:530 (Dec. 2) 1938. (*i*) Howitt, B. F.: Complement Fixation Test Differentiating Three Strains of Equine Encephalomyelitic Virus and the Virus of Lymphocytic Choriomeningitis, Proc. Soc. Exper. Biol. & Med. **35**:526 (Jan.) 1937. (*j*) Olitsky, P. K., and Harford, C. G.: Intraperitoneal and Intracerebral Routes in Serum Protection Tests with the Virus of Equine Encephalomyelitis: I. A Comparison of the Two Routes in Protection Tests, J. Exper. Med. **68**:173 (Aug.) 1938; (*k*) II. Mechanism Underlying the Difference in Protective Power by the Two Routes, ibid. **68**:761 (Nov.) 1938; (*l*) III. Comparison of Antiviral Serum Constituents from Guinea Pigs Immunized with Active or Formolized Inactive Virus, ibid. **68**:779 (Nov.) 1938. (*m*) Sabin, A. B., and Olitsky, P. K.: Variations in Pathways by Which Equine Encephalomyelitic Viruses Invade the CNS of Mice and Guinea Pigs, Proc. Soc. Exper. Biol. & Med. **38**:595 (May) 1938. (*n*) King, L. S.: Studies on Eastern Equine Encephalomyelitis: I. Histopathology of the Disease in the Guinea Pig, J. Exper. Med. **68**:677 (Nov.) 1938. (*o*) Finkelstein, H.; Marx, W.; Bridges, W. H., and Beard, J. W.: Rate of Inactivation of Equine Encephalomyelitis Virus (Eastern) Relative to the H-Ion Concentration, Proc. Soc. Exper. Biol. & Med. **39**:103 (Oct.) 1939. (*p*) Remlinger, P., and Bailly, J.: Action of High Temperatures on Rapidly Dried Viruses of Aujesky's Disease and Encephalomyelitis, Compt. rend. Soc. de biol. **129**:460, 1938. (*q*) King, L. S.: Studies on Eastern Equine Encephalomyelitis: II. Pathogenesis of the Disease in the Guinea Pig, J. Exper. Med. **69**:675 (May) 1939; (*r*) III. Intraocular Infection with Fixed Virus in the Guinea Pig, ibid. **69**:691 (May) 1939; (*s*) Infection of the Mouse with Modified and Unmodified Strains of E.E.E. Virus, J. Bact. **39**:43 (Jan.) 1940. (*t*) Morgan, I. M.: Influence of Age on the Rate and Degree of the Response of Mice to E.E.E. Virus, ibid. **39**:43 (Jan.) 1940. (*u*) Kempfe, J. E., and Soule, M. H.: Effect of Phagocytes on E.E.E. Virus, ibid. **39**:42 (Jan.) 1940.

analytic centrifuge arranged for photography according to the method of Svedberg, Wyckoff [7d] examined tissues diseased with equine encephalomyelitis and concluded from the sedimentation constant that if the virus particle is spherical and has about the same density as has been found for proteins and other small viruses, it has a molecular weight in the neighborhood of 25,000,000 and a diameter around 40 millimicrons. Howitt [7e] found that viruses of both American strains, as well as their neutralizing antibodies, would pass the placental barrier of guinea pigs, while viruses of a larger Russian strain (Moscow 2) would not.

Hurst [7f] divided the course of infections produced experimentally with these viruses into the visceral and the central nervous system (neurotropic) phase; in the guinea pig there was some overlapping of these phases, but in the monkey they were separated by an interval of two or three days. In the visceral phase the virus was present in the blood in greatest amount, with no demonstrable disproportionate increase in the amount of virus at the site of inoculation, while the central nervous system phase occurred at the peak of antibody response in the blood stream. He concluded that intracerebral injection of the virus was always fatal in the monkey and that these animals, even after recovering from this infection introduced by other routes, were not immune to subsequent intracerebral inoculation. He stated that the virus does not pass directly from the blood stream into the cerebrospinal fluid but rather is carried by the blood from the site of inoculation to the nasal mucosae, whence it passes up the olfactory tracts to reach the subdural space.

A more recently isolated Argentine strain of encephalomyelitis virus seems to be immunologically identical with the western American strains, while one of the Russian strains (Moscow 2) [7g] exhibits distinct differences from either of the American strains. Beck and Wyckoff [7h] studied a strain recovered in Venezuela which was immunologically different from both American strains, though perhaps remotely related to the eastern American strains. Howitt found that a small amount of the eastern strain of the virus given intradermally would produce the typical form of the disease in experimental animals, as compared with the much larger amount necessary with the western strains, and stated that this might account in part for the relative ease of demonstrating the role played by mosquitoes in transmission of the eastern strains of the virus. Only relatively tremendous doses of the American strains were infective for guinea pigs when fed by stomach tube and were probably infective at all only because of regurgitation of infective material up to the lymphoid tissues of the nasopharynx or to the nasal mucosae, indicating that the infection probably cannot enter through the alimentary canal. At the height of the temperature response in the course of an infection with either of the American strains, equine encephalomyelitis virus may be recovered from the serum, the brain, the liver, the spleen, the kidneys,

the adrenals, the testes, the ovaries or the cervical and salivary glands of guinea pigs. The virus is probably most abundant in all hosts during the increase of fever at the onset of the disease.

Eastern, western and Moscow 2 strains of the virus were found to be resistant to freezing with either salt and ice or with solid carbon dioxide for half an hour, followed by drying in vacuo; in the dried condition, however, they lost their virulence after four or five months.[7g] The eastern strain was most resistant to acid, withstanding a hydrogen ion concentration of p_H 3.6 as compared with one of p_H 5.5 for the western strain and of p_H 5.8 for the Moscow 2 strain; all three types withstood exposure to alkaline solutions with hydrogen ion concentrations up to p_H 9.0. These encephalomyelitis viruses are not thermostabile, viability being reduced after about a month in an ice box, two weeks at room temperature or less than a week at 37 C., the length of time depending to some extent on the type of fluid in which the infected material is stored. A 50 per cent buffered solution of glycerin is found by most workers a satisfactory medium in which to keep tissues containing the virus and is recommended for use in preserving autopsy material which is to be tested later for virus content. Howitt[7l] suggested that the complement fixation reaction, using antigens prepared from infected brain tissues, might be of value in differentiating the various strains of encephalomyelitis viruses, as well as the virus of lymphocytic choriomeningitis (Armstrong and Lillie), provided strongly hyperimmunized serums and potent antigens are used.

Olitsky and Harford noted that 12 to 15 day old mice were as susceptible to intraperitoneal inoculation with high dilutions of either of the American strains of the virus as adult mice were to intracerebral inoculation and discovered that intraperitoneal injection of appropriate mixtures of living virus and hyperimmune rabbit serum produced a higher degree of protection in the mouse than if such mixtures were given intracerebrally.[7j] From this observation, they continued their experiments to show that small amounts of antiserum (hyperimmune rabbit serum) given intraperitoneally would protect young mice against subsequent relatively tremendous doses of potent virus given by the same or by the intramuscular route but had little or no protective effect if the virus was given intranasally or intracerebrally.[7k] They obtained similar results when they injected a mixture of virus and antiserum together at the various sites, indicating that the varying degrees of protective power of the antiserums thus demonstrated must depend in large part on the particular pathway the virus takes to the central nervous system and on whether or not this pathway includes the blood stream.

As the antiserum which had been used in these experiments was secured from animals immunized by the injection of live virus, these

investigators next carried out a similar set of experiments differing only in the use of antiserum which was obtained from guinea pigs immunized with inactive (treated with a solution of formaldehyde U. S. P. in wood alcohol and water) virus.[71] Guinea pigs immunized with either of these preparations have about the same high degree of resistance to potent virus injected intracerebrally. Their results were peculiar and unexpected, in that there was a striking difference found in the protective power of the two types of antiserums. While both types had about the same low degree of protective power in young mice when tested by intracerebral inoculation of the virus-antiserum mixtures, it was found that antiserum secured from guinea pigs immunized with the active (live) virus had a much higher content of antivirus substance when such mixtures were given intraperitoneally. Although there seems to be no adequate explanation for these results at present, Olitsky and Harford have assumed that they are due to quantitative or qualitative differences in the antivirus substances obtained by the two methods of immunization and are consistent with the hypothesis previously advanced that the content of the antivirus antibody is not necessarily proportional to the degree of resistance to infection.

Sabin and Olitsky [7m] have shown, by a study of partial sections of the entire central nervous system of mice, that in the great majority of instances virus injected intramuscularly or intraperitoneally was carried in the blood to the nasal mucosae and thence to the brain by the olfactory pathway. It seems fair to assume, therefore, that the immune reaction probably takes place in the circulating blood or the reticuloendothelial system.

The pathologic changes produced by the American strains of the virus do not appear to be specific, consisting in the main of varying degrees of congestion and edema of the brain and cord generally. The chief microscopic feature is a perivascular and meningeal infiltration with polymorphonuclear and mononuclear cells early in the course of the infection, with later disappearance of the former cells. In 1 human subject, the changes were most marked in the gray matter of the spinal cord, where about one third of the nerve cells in the cervical segment were in various stages of disintegration. Small intranuclear inclusion bodies have been observed occasionally in animals with experimentally produced infections, particularly in the developing embryonic nerve cells of the chick, but have not been noted in human material. In the group of cases reported by Feemster,[3] the blood showed leukocytes (more than 14,600 cells) with 75 to 90 per cent polymorphonuclear cells. Early in the disease the spinal fluid was found to be under increased pressure, with an elevated protein content, normal or slightly increased values for sugar and a cell count varying from 200 to 2,000 per cubic millimeter, 60 to 90 per cent of which were polymorphonuclear cells. In the patients living

over two or three days there was a drop in the number of leukocytes in both spinal fluid and blood, with a change to the mononuclear type.

In addition to the known infectivity for horse and man [8] of both American varieties of these encephalomyelitis viruses, it has been found that they are also capable of producing disease in a wide variety of other mammals and in birds, under experimental as well as under natural conditions; [9] thus the qualifying adjective "equine" serves only to confuse the terminology. The ease with which the infection can be induced experimentally in mice and in guinea pigs, the large number of birds proved susceptible to the encephalomyelitis viruses and the recovery of the eastern strain of equine virus from the brains of pigeons and ring-necked pheasants dying under natural conditions, all suggest the need for a survey of rodents and migratory birds in an attempt to define the true reservoir of the disease in nature.

Epidemiologic observations have incriminated the mosquito, the common tick, Dermacentor andersoni, and possibly the horsefly as the most important insect vectors.[10] In 1933, Kelser [10a] proved that the mosquito

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9. (*a*) Syverton, J. T., and Berry, G. P.: Susceptibility of the "Gopher," Citellus Richardsoni (Sabine) to Equine Encephalomyelitis, Proc. Soc. Exper. Biol. & Med. **34**:822 (June) 1936. (*b*) Wyckoff, R. W. G.: Encephalomyelitis in Monkeys, Science **89**:542 (June 9) 1939. (*c*) Tyzzer, E. E.; Sellards, A. W., and Bennett, B. L.: The Occurrence in Nature of Equine Encephalomyelitis in the Ring-Necked Pheasant, ibid. **88**:505 (Nov. 25) 1938. (*d*) Fothergill, L. D., and Dingle, J. H.: A Fatal Disease of Pigeons Caused by the Virus of the Eastern Variety, ibid. **88**:549 (Dec. 9) 1938. (*e*) Davis, W. A.: Experiments on the Role of Birds and Mosquitoes in the Epidemiology of E.E., J. Bact. **39**:42 (Jan.) 1940. (*f*) Remlinger, P., and Bailly, J.: Transmission of Equine Encephalomyelitis, Compt. rend. Soc. de biol. **120**:1067, 1935; **121**:146, 1936; **122**:518, 1936; **123**:562, 1936.

10. (*a*) Kelser, R. A.: Mosquitoes as Vectors of the Virus of Equine Encephalomyelitis, J. Am. Vet. M. A. **82**:767 (May) 1933. (*b*) Merrill, M. H.; Lacaillade, C. W., and Ten Broeck, C.: Mosquito Transmission of Equine Encephalomyelitis, Science **80**:251 (Sept. 14) 1934. (*c*) Merrill, M. H., and Ten Broeck, C.: Multiplication of Equine Encephalomyelitic Virus in Mosquitoes, Proc. Soc. Exper. Biol. & Med. **32**:421 (Dec.) 1934. (*d*) Syverton, J. T., and Berry, G. P.: An

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Aedes aegypti could transmit the virus from animal to animal, the insects being infectious from at least the sixth to the eighteenth day after engorging on an infected host. Altogether, eight species of the genus Aedes have been found capable of transmitting the virus under experimental conditions, though no one has isolated the virus from mosquitoes in nature. Although work on this phase of the problem is still incomplete, it seems to have been established that the eastern strains of the virus may be transmitted by A. cantator and the western by A. aegypti, A. albopictus, A. nigromaculis, A. dorsalis, A. vexans and A. taeniorhyncus, while A. collicitans may carry either variety. Merrill, Lacaillade and Ten Broeck [10b] suggested that the different vectors for the two strains may explain some of their serologic differences. They stated that if a mosquito was to act as a vector, it must be fed on infected animals at a time when the virus content of the blood is such that 0.0001 cc. or less will produce the disease when injected into a guinea pig. In 1 instance the bite of a single A. aegypti mosquito transmitted virus of the western strain to a guinea pig. The virus is not merely carried mechanically by the mosquitoes, as titration experiments with ground suspensions of these insects have shown an increase (multiplication, maturation or cyclic change) in the virus within five days. The virus does not kill the mosquitoes and seems to be generally distributed in their bodies, their body fluid and ground suspensions of their legs, heads, thoraxes or abdomens all being about equally infective. Merrill and Ten Broeck [10c] found no serologic change in the virus after passage through ten lots of mosquitoes. It appears that the virus persists in some of the mosquitoes as long as they live, some of the insects being infective for as long as sixty-three days; virus was recovered from such a lot of mosquitoes ninety-three days after feeding, though at this time they did not transmit the disease.

Syverton and Berry [10d] found that the common tick, D. andersoni, could transmit the western strain of the virus under experimental conditions, but this particular insect is not found in the late summer and early fall, when encephalomyelitis has its highest incidence. These same investigators demonstrated [9a] that the common ground squirrel, or gopher (Citellus richardsoni), would contract the disease from the bite of an infected tick or from the intranasal instillation of the virus. This

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Arthropod Vector for Equine Encephalomyelitis, Western Strain, Science **84**:186 (Aug. 21) 1936. (*e*) Madsen, D. E., and Knowlton, G. F.: Mosquito Transmission of Equine Encephalomyelitis, J. Am. Vet. M. A. **86**:662 (May) 1935. (*f*) Simmons, J. S.; Reynolds, F. H. K., and Cornell, V. H.: Transmission of the Virus of Equine Encephalomyelitis Through Aedes Albopictus, Skuze, Am. J. Trop. Med. **16**:289 (May) 1936. (*g*) Kelser, R. A.: Transmission of the Viruses of Equine Encephalomyelitis by Aedes Taeniorhyncus, Science **85**:178 (Feb. 12) 1937; (*h*) Transmission of the Virus of Equine Encephalomyelitis by Aedes Taeniorhyncus, J. Am. Vet. M. A. **92**:195 (Feb.) 1938.

animal's symptoms after infection are similar to those seen in the more common laboratory rodents. However, the virus has not been recovered from gophers under natural conditions.

Various "live" and "killed" vaccines have been prepared from virus either secured directly from the brains of infected animals or grown on chick embryos.[11] The latter appears to be the most suitable medium for cultivation of the virus, and chick embryo vaccine treated with a solution of formaldehyde U. S. P. in wood alcohol and water seems to be the most effective protective agent. Passive immunity induced by the use of convalescent or hyperimmune horse serums appears to be too short lived, too costly and too difficult to evaluate to warrant the extensive use of these serums in prophylaxis. Hyperimmune horse serum is probably of value if given in large doses intravenously in the early stages of the disease in horses. Wyckoff [9b] found that hyperimmune horse serum protected monkeys against virus introduced intranasally but had no therapeutic value if given after the onset of fever. Crude chick embryo vaccine seemed to be an effective prophylactic agent against massive doses of either variety of the virus given intranasally to these animals. The value of vaccination for human beings is not known.

Three cases of equine encephalomyelitis have been reported in laboratory workers, 2 fatal.[12] Olitsky and Morgan [12a] were able to demonstrate the presence of protective antibodies in the serum of only 1 of 6 laboratory workers who had been intimately associated with work on the eastern strains of the virus for periods varying up to six years. This person had never had any illness resembling encephalomyelitis. Such an observation, therefore, lends additional support to the general belief that numerous subclinical or abortive types of this disease may occur in any susceptible group.

During the summer of 1938, there were 23,686 cases of equine encephalomyelitis reported by the veterinarians of Minnesota, with 4,979 deaths. In Jackson County, where the case in a child which is

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11. Beck, C. E., and Wyckoff, R. W. G.: The Antigenic Stability of Western Equine Encephalomyelitic Virus, Science **88**:264 (Sept. 16) 1938. Mitchell, C. A.; Walker, R. V. L., and Plummer, P. J. G.: Studies in Equine Encephalomyelitis: Chick Embryo Vaccine as a Protective Agent, Canad. J. Comp. Med. **2**:211 (Aug.) 1938. Eichorn, A., and Wyckoff, R. W. G.: Immunologic Studies in Equine Encephalomyelitis, J. Am. Vet. M. A. **93**:285 (Nov.) 1938. Records, E., and Vawter, L. R.: Equine Encephalomyelitis Antiserum, ibid. **92**:608 (April) 1938.

12. (*a*) Olitsky, P. K., and Morgan, I. M.: Protective Antibodies Against Equine Encephalomyelitis in the Serum of Laboratory Workers, Proc. Soc. Exper. Biol. & Med. **41**:212 (May) 1939. (*b*) Fothergill, L. D.; Halden, M., and Wyckoff, R. W. G.: Western Equine Encephalomyelitis in a Laboratory Worker, J. A. M. A. **113**:206 (July 15) 1939. (*c*) Helwig, F. C.: Western Equine Encephalomyelitis Following Accidental Inoculation with Chick Embryo Virus, ibid. **115**: 291 (July 27) 1940.

reported here originated, there were 495 presumptive cases in horses, with 88 deaths.[13] Eklund and Blumstein[14] have studied 35 cases of encephalitis which occurred in human beings in Minnesota during August and September 1938, and positive neutralization for western strains of the equine encephalomyelitis virus was demonstrated in 11 of these. Three species of Aedes proved capable of transmitting the western strains of encephalomyelitis viruses are known to exist in Minnesota; A. vexans is the most common species of the genus and may be found as late as October.[15]

REPORT OF A CASE

D. D., a boy, was first admitted to the pediatric department of the University Hospitals at the age of 5 months for study of convulsive seizures and irritability of three months' duration. The mother, an intelligent and careful observer, stated that her pregnancy and labor had been uneventful and that the infant had appeared to be normal until he was 4 weeks old. These statements were verified by others, including the physician who cared for the mother during pregnancy, delivered the infant and observed the initial febrile episode to be described. The mother had suffered no illness even remotely suggestive of encephalomyelitis.

On September 13, when 4 weeks old, the infant suddenly became ill, with high fever and extreme irritability as outstanding manifestations. He was admitted to a hospital, where transitory strabismus was noted. He had a sustained high temperature, and frequent generalized convulsions developed, which decreased in frequency and severity with the gradual subsidence of the fever after one week. No study was made of the spinal fluid, but because of the presence of high fever, irritability and convulsions without any discernible infection, a presumptive diagnosis of encephalitis was made. After ten days, he was discharged from the hospital in apparently good condition, and for the next month at home he seemed entirely well.

Beginning at the age of about 2 months or shortly after, and approximately a month after the initial febrile illness, his parents noted the onset of peculiar mild "jerking spells" of momentary duration but of gradually increasing frequency. These consisted of a sudden twisting of the head to one side or the other, with rapid flexion of the arms and extension of the legs. Such seizures occurred as often as ten times in twenty-four hours and seemed to cause the infant no pain or discomfort. They were most apt to occur when he had suddenly been disturbed for any reason. In other respects the baby seemed normal.

Suddenly, on December 23, seven weeks after the original febrile episode, which had been diagnosed as possible encephalitis, these seizures became more severe and prolonged, each one causing the infant to cry out as though in pain. He assumed an "arched position" (opisthotonos) most of the time, and the extremities, particularly the legs, became spastic. With the increase in spasticity, the convulsive seizures became more frequent and more prolonged. Extreme irritability

13. Cotton, C. E., Executive Secretary Minnesota State Live Stock Sanitary Board: Personal communication to the author.

14. Eklund, C. M., and Blumstein, A.: To be published.

15. Owen, W. B.: The Mosquitoes of Minnesota, with Special Reference to Their Biology, Technical Bulletin 126, University of Minnesota Agricultural Experiment Station, November 1937.

and restlessness were evident until the infant was admitted to the hospital about one month later. Throughout this period there had been no fever or other sign of infection.

During the latter part of August and the early part of September, there had been an unusually large number of insects in the apartment in which the family resided. The mother attributed this to the fact that the occupants of an adjoining apartment were in the business of trucking livestock from neighboring farms to the packing plants a short distance away. She assumed that these persons had carried a large number of insects on their clothing, particularly as she had noted many horseflies in the building just after the truckers had returned from work each day. In spite of all precautions, the mother was certain that the infant had been bitten on several occasions by mosquitoes as well as by horseflies.

When he was admitted to the hospital, the infant appeared well developed, with normal nutrition and with body measurements showing no significant aberration from normal figures for the age of 5 months. He weighed 6.9 Kg.; his total length was 64 cm.; the circumference of his head was 41.5 cm. and that of his chest 42 cm. The anterior fontanel was fibrous and measured 1.5 cm. in its greatest diameter. The rectal temperature was 38 C. (100 F.), and the respirations were normal in rate and character. The pulse was variable, the rate being about 110 per minute at rest, with rapid acceleration coincident with or immediately following each convulsion. He was extremely irritable and was having innumerable convulsions as previously described, each one lasting from three to eight minutes, initiated by a strong "cerebral" cry and followed by the assumption of a position of decerebrate rigidity with full opisthotonos, extreme hypertonicity, extension of the legs with strong plantar flexion of the feet, acute flexion of the arms and rotation of the head, usually to the right. There was no clonic phase, simply slow relaxation of the hypertonicity. Though most of these seizures seemed to occur spontaneously, they could be regularly induced by any slight stimulus, except during a short refractory period of a minute or two following each one. There was generalized symmetric hyperreflexia. Bilateral, well sustained ankle clonus could be elicited, and there was dorsiflexion of the great toe, with "fanning" of the others, on plantar stimulation. The tonic neck reflex (Magnus-de Kleijn) was positive, and when the infant was held erect his legs assumed the "scissors position." The pupils reacted to light, the infant's eyes followed a moving object well and ophthalmoscopic examination showed the fundi to be normal. The remainder of the general physical examination revealed no abnormalities, in particular no evidence of any deficiency disease, tuberculosis, tetany or lead poisoning.

Urinalysis showed nothing unusual. The hemoglobin level was 12 Gm. per hundred cubic centimeters (71 per cent, Sahli). There were 10,300 leukocytes per cubic millimeter of blood, with 42 per cent neutrophils, 56 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils. The fasting blood sugar was 102 mg. per hundred cubic centimeters, and the carbon dioxide–combining power of the plasma was 53 volumes per cent. The serum calcium was 11.6 mg. per hundred cubic centimeters, and the phosphorus, 5.7 mg. All of these analyses were repeated later, and the results showed no significant change. The reactions to the Mantoux and Schick tests were negative. The Wassermann reaction of the blood was negative on two occasions. An electrocardiogram was made because of the striking and rapid increase in pulse rate with each convulsion, but this showed no abnormality. The spinal fluid was clear and colorless, was under a pressure of 12 mm. of mercury and contained 2 mononuclear cells per cubic millimeter; the protein level was 24.4 mg. per hundred cubic centimeters; sugar, 85 mg., and chlorides, 706 mg. There were no organisms on direct examination, the reactions

to the Wassermann and the Kahn tests were negative and routine cultures remained sterile. An encephalogram, made by replacing 60 cc. of cerebrospinal fluid with air, using the lumbar approach, showed a moderate symmetric dilatation of the ventricular system, with slight widening of the subarachnoid space, indicative of some degree of diffuse cerebral atrophy (figure, *A*).

During this period of hospitalization, or approximately six months after the onset of the original acute illness, a specimen of blood serum was submitted for determination of the antivirus antibody content.[16] The protective power of this

Encephalograms of D. D. *A*, at 6 months, and *B*, at 18 months of age.

serum against both the eastern and the western strains of equine encephalomyelitis virus was determined by the technic of Olitsky and Harford,[7k] which consists of the intraperitoneal injection into young mice (9 to 16 days of age) of mixtures of the unknown serum with graded dilutions of a known virus suspension. By comparison with a similar series of mice into which mixtures containing normal serum are injected, the presence of protective antibodies against the specific strain

16. The determination was made by Dr. F. Howell Wright, of the Rockefeller Institute for Medical Research.

of the virus can be recognized and qualitatively measured in terms of the number of minimum lethal doses against which it will protect. The test is further controlled by running tests with the homologous hyperimmune rabbit serum in parallel.

Neutralization tests against the virus of St. Louis encephalitis were also run, using the standard technic in which similar mixtures are injected intracerebrally into mice about 4 weeks of age.

Since there was a possibility that this infant might have acquired antibodies by placental transmission from the mother during pregnancy,[7n] a specimen of maternal blood serum was also examined for protective power against the strains of equine encephalitis virus. The table lists the results obtained in these tests,

Results of Neutralization Tests Against Encephalitis Viruses

Test No.*	Type of Encephalitis Virus	Serum	Highest Dilution of Virus Fatal for Mice	No. of Minimum Lethal Doses Against Which Serum Protects
1	Western strain of "equine"	Normal control	10^{-3}	
		Patient	$<10^{-4}$	At least 10,000
		Immune rabbit	$<10^{-2}$	At least 1,000,000
2	Western strain of "equine"	Normal control	10^{-7}	
		Patient	$<10^{-2}$	At least 100,000
		Immune rabbit	$<10^{-2}$	At least 100,000
3	Western strain of "equine"	Normal control	10^{-7}	
		Patient	10^{-2}	10,000
		Immune rabbit	$<10^{-2}$	At least 100,000
4	Eastern strain of "equine"	Normal control	10^{-7}	
		Patient	10^{-7}	0
		Immune rabbit	10^{-2}	10,000
5	Eastern strain of "equine"	Normal control	10^{-3}	
		Patient	10^{-7}	1
		Immune rabbit	10^{-2}	At least 1,000,000
6	St. Louis	Normal control	10^{-4}-10^{-5}	
		Patient	10^{-4}	<1
		Immune rabbit	10^{-2}-10^{-3}	10 to 100
7	Western strain of "equine"	Normal control	10^{-7}	
		Patient's mother	10^{-7}	0
		Immune rabbit	$<10^{-2}$	At least 100,000
8	Western strain of "equine"	Normal control	10^{-6}	
		Patient's mother	10^{-7}-10^{-8}	<1
		Immune rabbit	$<10^{-2}$	At least 1,000,000
9	Eastern strain of "equine"	Normal control	10^{-3}	
		Patient's mother	10^{-7}	1
		Immune rabbit	$<10^{-2}$	At least 1,000,000

* Tests 1 to 6 were performed during the patient's first period of hospitalization, tests 7 to 9 during the second period.

that is, a high titer of antibodies against the western strain of the virus and none against the eastern or St. Louis types. The mother's serum furnished no protection against either strain of equine encephalitis virus.

During seventeen days in the hospital, there was no significant change in the infant's condition; there was a gain in weight of approximately 500 Gm., and the convulsive episodes, extreme irritability and hypertonicity were all considerably relieved by frequent sedation with phenobarbital. He was then discharged, to be under further observation in the outpatient department, where he was seen frequently until the age of 10 months. During that period there was no great change in the character of the convulsive seizures, though it soon became apparent both to the physicians and to the parents that there was a marked delay in mental development, probably actual deterioration.

The infant failed to gain weight normally and because of extreme irritability and tonic convulsions at the slightest disturbance became an almost unmanageable problem in the home. Accordingly, at the age of 10 months, he was readmitted to the hospital, primarily in an attempt to adjust his feeding difficulties and schedule of sedation. Repetition of laboratory studies at this time showed no significant variation in results from those previously secured. At the age of a year, he weighed 8.5 Kg.; his total length was 75 cm.; the circumference of his head was 42.5 cm., of his chest 45 cm. and of his abdomen 39 cm. The anterior fontanel was closed.

At the age of 18 months, one year after the first encephalogram was made, encephalographic studies were repeated (figure, *B*) with a roughly comparable technic. These showed some increase in the size of the ventricles, failure of filling of the subarachnoid or subdural space on the right side and increase in the width of this space on the left side. These changes suggest the presence of progressive cerebral atrophy and possibly obliterative subarachnoid adhesions on the right.

At 2½ years of age, this infant appears to have shown no appreciable increase in mental development since he was first studied, at the age of 5 months. He now weighs 10.7 Kg. and is 80 cm. long; the circumference of his head is 44 cm., of his chest 47 cm. and of his abdomen 43 cm. There are six teeth. There are almost continuous opisthotonos, marked spasticity of all muscles and generalized symmetric hyperreflexia. Hirsuties is becoming more prominent over the entire body, together with an indefinite "tanned" appearance not related to exposure to the sun. Vision and hearing are difficult to evaluate in view of the obvious mental deficiency but seem to be seriously impaired. Optic atrophy is obvious on ophthalmoscopic examination. In spite of almost continuous rather heavy sedation, tonic convulsions of momentary duration continue to occur at about half hour intervals.

SUMMARY AND CONCLUSIONS

Equine encephalomyelitis is a specific virus infection affecting a variety of animals, including man. Young subjects are most susceptible. The natural reservoir of the disease has not yet been recognized. Mosquitoes and ticks are the only insects proved capable of acting as vectors. The virus exists in the United States in at least two immunologically distinct strains, which are rather sharply demarcated geographically by the Appalachian Mountains.

Experimentally, the course of infection with either of the American strains can be divided roughly into visceral and neurotropic phases. Under natural conditions the disease in many cases may go unrecognized as abortive or poorly defined visceral manifestations.

The American encephalomyelitis viruses have been intensively studied in a number of laboratories. Their size, their resistance to various physical and chemical agents, their infectivity for laboratory animals and the pathologic changes they produce under natural and experimental conditions have been recorded. The virus is best cultivated on the chorioallantoic membrane of the developing chick. Chick embryo vaccine treated with a solution of formaldehyde U. S. P. in wood alcohol and water seems well established as the most practical and effective prophylactic agent for control of the disease in horses, but has not as yet been used

for the human subject. Hyperimmune serums apparently have no value in the therapy of infections experimentally produced when given after the onset of fever.

A case illustrating the postencephalitic state, most probably an aftermath of infection with the virus of "equine" encephalomyelitis, is presented. The diagnosis was established by the demonstration of a high titer of antivirus antibodies for the western strain in the patient's serum six months after the initial acute infection. The mother's serum contained no protective substances against this virus.

This report emphasizes the need for considering equine encephalomyelitis in the differential diagnosis of the large group of obscure neurologic disorders in which mental retardation and spasticity are outstanding manifestations.

News and Comment

GENERAL NEWS

Investigations in Gerontology.—The National Institute of Health, of the United States Public Health Service, is organizing a new unit for research into some of the many problems of aging. With the conspicuous shift to greater age in the population, senescent persons are becoming increasingly significant in the national economy and defense. Preventive medicine must attack the practical problems of the rising proportion of deaths attributable to diseases of middle age and later life and energetically attempt to augment the health and vigor of those persons who are past the meridian of life. Aging is a continuous biologic phenomenon, which starts on creation of a new person and continues at variable rates until death. The problems of aging (gerontology) are not limited to the diseases of the aged (geriatrics), for the latter are the consequences of senescence. In man, probably the most significant period of life for gerontologic study is late maturity, approximately the two decades between 40 and 60.

The problems of aging are logically divisible into three major fields of investigation: (1) the biology of senescence as a process, (2) the human clinical problems of aging and of the diseases characteristically associated with advancing years, which include the mental, as well as the physical, changes of senescence and senectitude, and (3) the socioeconomic problems of a shifting age distribution in the population. The National Institute of Health is concerned with the first two divisions of this subject.

In order to advise this new unit, there has been formed a National Advisory Committee on Gerontology, which is representative of the scientific thought of the nation. The membership of this advisory committee includes: Dr. L. R. Thompson, director of the National Institute of Health, United States Public Health Service; Dr. Anton J. Carlson, physiologist, University of Chicago, member of the National Research Council; Dr. Charles L. Christiernin, Association of Life Insurance Medical Directors of America, medical director of the Metropolitan Life Insurance Co.; Dr. Robert A. Coker, zoologist, University of North Carolina; Dr. William Crocker, botanist, Boyce Thompson Institute of Plant Research; Mr. Lawrence K. Frank, sociologist, Josiah Macy Jr. Foundation; Dr. A. Baird Hastings, biochemist, Harvard University; Dr. Ludvig Hektoen, pathologist, consultant to the National Cancer Institute, United States Public Health Service; Dr. Winfred Overholser, psychiatrist, superintendent of St. Elizabeths Hospital; Dr. Clarence Selby, industrial physician, General Motors Corporation, and Dr. William D. Stroud, clinician, Philadelphia.

The first service to scientific research which the unit on gerontology is undertaking is a survey of the present trends of existent and contemplated investigations in American scientific institutions into the problems of aging. This survey is intended to ascertain just what problems are being studied and what methods of approach are being applied. There is no desire to learn in advance of publication the data being gathered in these specific undertakings.

In addition to these studies, many investigations which do not pertain directly to problems of aging should yield data useful to workers in gerontology. The unit on gerontology is especially interested in knowing of these indirectly related studies, the full implications of which are far too often obscured in their published titles.

Inquiries about studies related to aging are being sent to investigators in the basic biologic sciences as well as to clinical investigators, for much fundamental work on the processes, mechanisms and consequences of senescence is probably going on in such fields as botany, zoology, physiology, pharmacology and psychology. From the clinical point of view, the greatest concern is with those studies dealing with the evaluation of health and the mensuration of functional capacity (including criteria of "physiologic age") and with those diseases of which the incidence increases sharply in later life (the so-called "degenerative disorders").

Critical analysis of the information elicited by such a survey may be expected to serve several valuable purposes. It should assist in bringing together in closer cooperation investigators interested in related problems, especially those who are utilizing widely divergent methods of approach. The survey will likewise emphasize the urgent need for greatly augmented support for significant studies of these vitally important problems of senescence.

The broad and general pattern of the problems being investigated will undoubtedly reveal a number of neglected "blank spots" which may justify special emphasis in the future. Analysis of the data of the survey will also be an invaluable aid in formulating future research programs, both at the National Institute of Health and elsewhere.

From preliminary inquiries, it is observed that there is a great, but largely latent and scattered, interest in the problems of aging. It is the hope of the unit of gerontology of the National Institute of Health that the present survey may effectively aid in the promotion of closer cooperation of the scientists interested in these fields.

Information concerning the subjects under investigation and the methods of approach is earnestly solicited. Letters should be addressed to:

Dr. Edward J. Stieglitz,
In charge Investigations in Gerontology,
National Institute of Health, United States Public Health Service, Bethesda, Md.

SOCIETY NEWS

Georgia Pediatric Society.—The annual scientific meeting of the Georgia Pediatric Society will be held in Atlanta on December 12, beginning with a luncheon at 12:30 p. m. An afternoon and an evening session will be held, in the Pompeian Ballroom of the Atlanta Biltmore Hotel. The following papers will be read: "The Prognostic Value of Renal Function Tests in Nephritis" and "The Role of Diet in the Therapy of Nephritis," by Lee Edward Farr, M.D., director of research of the Alfred I. DuPont Institute; "The Handicaps of Prematurity and How to Meet Them" and "Water and the Growing Organism," by Samuel Zachary Levine, M.D., professor of pediatrics, Cornell University Medical College, and "The Manifestations of Rheumatic Fever in Childhood" and "The Course of Rheumatic Heart Disease in Childhood and Adolescence," by Edward F. Bland, M.D., instructor of medicine, Harvard Medical School, and assistant physician, Massachusetts General Hospital.

PERSONAL NEWS

Appointment Announced.—On the retirement of Dr. Joseph Brennemann, on Jan. 1, 1941, as medical director of the Children's Memorial Hospital, Chicago, Dr. C. A. Aldrich, of Winnetka, Ill., will assume the position.

Correspondence

IMMUNIZATION AGAINST PERTUSSIS

To the Editor:—The recent publication by Doull and his associates [1] of the final results of their study of pertussis prophylaxis again brings out the sharp contrast between their results and those obtained by a number of other workers in the same field and renews the confusion felt by many physicians when attempting to judge the merits of vaccination against pertussis. The matter is one of prime importance in pediatrics and preventive medicine, since if vaccination for whooping cough is meritorious it should be generally employed. For this reason, we submit a brief summary of such published work as is now available.

Besides the work of Doull and his collaborators, there are seven separate studies [2] which fulfil, as does the investigation of Doull and his associates, the following requirements: (1) The vaccine used was made from Haemophilus pertussis in phase 1 (Leslie-Gardner classification); (2) the total dosage was

TABLE 1.—*Attack Rates for Children Vaccinated and Unvaccinated Against Pertussis*

	Vaccinated Children			Unvaccinated Children		
	Number Vaccinated	Number Contracting Pertussis	Per Cent Contracting Pertussis	Number Observed	Number Contracting Pertussis	Per Cent Contracting Pertussis
Doull and associates [1].....	381	65	17.05	496	94	18.95
Other investigators [2].....	6,483	129	1.98	5,999	846	14.10

75,000,000,000 organisms or more, and (3) a satisfactory number of unvaccinated controls was studied during the same period of observation and in the same place. Further, for all the series except two of Siegel's three small groups the vaccine was prepared from fairly recently isolated cultures. The results of the seven studies, comprising observations on over 12,000 subjects, are fairly harmonious with each other and in disagreement with those of Doull and his associates. They are, therefore, combined in table 1 for comparison with the figures obtained by Doull and his co-workers.

1. Doull, J. A.; Shibley, G. S.; Haskins, G. E.; Bancroft, H.; McClelland, J. E., and Hoelscher, H.: Active Immunization Against Pertussis, Am. J. Dis. Child. **58**:691 (Oct.) 1939.

2. (*a*) Howell, C.: Prophylactic Use of Pertussis Vaccine (Sauer), South. M. J. **31**:1166, 1938. (*b*) Siegel, M.: Active Immunization Against Whooping Cough with Various Specific Vaccines, Am. J. Dis. Child. **56**:1294 (Dec.) 1938. (*c*) Singer-Brooks, C.: A Controlled Study of Pertussis Prophylaxis, J. Pediat. **14**:25, 1939. (*d*) Sauer, L. W.: Whooping Cough, J. A. M. A. **112**:305 (Jan. 28) 1939. (*e*) Kendrick, P., and Eldering, G.: A Study of Active Immunization Against Pertussis, Am. J. Hyg. (Sect. B) **29**:133, 1939. (*f*) Silverthorne, N.: Active Immunization Against Whooping Cough, Canad. M. A. J. **41**:263, 1939. (*g*) Miller, J. J., Jr., and Faber, H. K.: Immunization Against Pertussis, J. A. M. A. **112**:1145 (March 25) 1939.

The communicability rate (incidence of pertussis after exposure) is perhaps a somewhat more rigid criterion of the effectiveness of vaccination than is the attack rate (incidence of pertussis in a given group). Figures on communicability were given in five [3] of the seven series, but Doull and his co-workers gave data only for household exposures. For the five series the communicability rate for all exposures was 16.92 per cent for the vaccinated children as compared with 80.25 per cent for the unvaccinated children. Figures were given in four [4] of these studies for household exposures, and to them, in table 2, we have added figures from an earlier study of Sauer [5] (which are not included in his later paper) and from his 1939 study [2d] to make up the combined data for comparison with the data of Doull and his associates.

It is obvious (and we have confirmed this by statistical analysis by Fisher's chi square method) that the differences between rates for vaccinated and those for unvaccinated children in the combined series are significant and could not occur by chance, whereas the opposite is true of the rates for the series of Doull and his associates. We therefore feel fully justified in drawing the following conclusions: (1) that the vaccine employed by the investigators whose results we

TABLE 2.—*Communicability Rate for Household Exposures to Pertussis*

	Vaccinated Children			Unvaccinated Children		
	Number Exposed	Number Contracting Pertussis	Per Cent Contracting Pertussis	Number Exposed	Number Contracting Pertussis	Per Cent Contracting Pertussis
Doull and associates [1].....	73	56*	76.71	62	61	98.39
Other investigators [6].....	183	42	22.35	226	203	89.80

* Twelve other children of the series had "atypical coughing and may have had abortive attacks." If these were added to the number contracting the disease (and such patients were included in arriving at our own figures), the communicability rate in the series of Doull and his associates would be 93.15 per cent. Their inclusion would also raise the attack rate for vaccinated children, given in table 1, to 20.21 per cent.

combined and considered as a unit was effective in preventing pertussis and (2) that the vaccine employed by Doull and his associates was ineffective.

While the success of immunization against pertussis with the dosages now generally used is not quite comparable to that of immunization against diphtheria and smallpox in completeness and percentage of subjects protected, it appears to us that the 78 per cent protection attained with good pertussis vaccine, as shown in table 2, is high enough to justify general adoption of the method and its inclusion in the routine program of immunization for infants and young children.

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3. Siegel.[2b] Singer-Brooks.[2c] Kendrick and Eldering.[2e] Silverthorne.[2f] Miller and Faber.[2g]

4. Siegel.[2b] Singer-Brooks.[2c] Kendrick and Eldering.[2e] Miller and Faber.[2g]

5. Sauer, L. W.: Immunization with Bacillus Pertussis Vaccine, J. A. M. A. **101**:1449 (Nov. 4) 1933.

6. Siegel.[2b] Singer-Brooks.[2c] Sauer.[2d] Kendrick and Eldering.[2e] Miller and Faber.[2g] Sauer.[5]

Abstracts from Current Literature

Biochemistry, Bacteriology, and Pathology

BIOLOGICAL FACTORS INVOLVED IN THE BACTERICIDAL IRRADIATION OF AIR. WILLIAM FIRTH WELLS, J. Bact. **39**:18 (Jan.) 1940.

The author states that "quantitative technics for suspending microorganisms in air and for determining the changes in concentration have provided the means for studying the bactericidal irradiation of air. The bactericidal action of ultraviolet rays upon organisms suspended in dry air was of a different order of magnitude from that which obtained when they were suspended in water or distributed on moist agar surfaces. The disinfection rate in dry air was many times greater than that in moist air. The death rate of most vegetative bacteria was approximately constant for significant disinfection ranges. These death rates have been determined. A technic for separating bacteria in air suspensions so that no particle contains more than one organism has been developed. The death rate of Sarcina lutea packets of fixed numbers conformed to that resulting from the single cells. The effectiveness of bactericidal rays against bacteria in association with particles of dust was much reduced."

STOESSER, Minneapolis.

A STUDY OF A SEROLOGICAL PRINCIPLE FOR THE SEPARATION OF MIXTURES OF BACTERIAL SPECIES, WITH PRELIMINARY APPLICATION TO THE ISOLATION OF TYPHOID BACILLI FROM FECES. J. H. HANKS, R. B. HOULIHAN and L. W. PARR, J. Infect. Dis. **66**:33 (Jan.-Feb.) 1940.

"In a mixture of bacterial species, serum sensitization of the predominating organisms was found to promote greatly the isolation of unsensitized bacterial species."

FROM AUTHORS' SUMMARY.

STUDIES ON LISTERELLA: I. A LISTERELLA STRAIN ISOLATED FROM A PREMATURE BOVINE FETUS. R. GRAHAM, H. R. HESTER and N. D. LEVINE, J. Infect. Dis. **66**:91 (Jan.-Feb.) 1940.

"A pregnant heifer aborted following the inoculation of a strain of Listerella isolated from an aborted bovine fetus. Listerella was recovered from the fetus, but not from the placenta, colostrum or vaginal discharges of the heifer. The heifer recovered.

"Attempts to induce abortion in pregnant rabbits, guinea pigs, and swine by inoculation of the same strain of Listerella failed.

"This strain of Listerella caused temporary illness when inoculated intravenously into a non-pregnant heifer. Similar inoculation of a six-weeks old pig produced death in 3 days. Rabbits and guinea pigs inoculated with the same strain died in a few days.

"Conjunctivitis was produced in rabbits and guinea pigs by instillation of this Listerella into the conjunctival sac. Massive necrosis of the myocardium was produced in chickens by intravenous inoculation."

AUTHORS' SUMMARY.

THE LANCEFIELD GROUPS OF HEMOLYTIC STREPTOCOCCI FOUND IN CHILDREN. E. ESTRADA, Yale J. Biol. & Med. **12**:407, 1940.

One hundred strains of hemolytic streptococci were recovered in the routine culture of material from 475 children in the pediatric service of a general hospital and dispensary. Ninety of these strains belonged to Lancefield's group A, 6 to

group C and 1 to group F. All strains associated with obvious streptococcic disease (such as scarlet fever and erysipelas) were of group A, and 88 of the 93 children carrying them were sick with or convalescent from attacks of streptococcic disease, rheumatic fever, chorea or nephritis. It appeared that the carrier state in respect to streptococci of group A had special clinical significance in the pediatric service in the locality of the study. J. D. TRASK, New Haven, Conn.

Metabolism; Infant Feeding; Milk and Other Foods

IRON METABOLISM: I. THE ROLE OF CALCIUM IN IRON ASSIMILATION. S. W. KLETZIEN, K. W. BUCHWALD and L. HUDSON, J. Nutrition **19**:187 (Feb.) 1940.

An interesting experiment on young rats is reported. The animals were fed a milk diet productive of severe anemia; then the effect of variation in the supply of calcium on the amount of iron in the various organs and in the entire body was studied. It was noted that with the addition of various calcium salts to the diet (i. e., calcium carbonate, lactate, chloride, triphosphate and sulfate) the calcium exerted an adverse effect on iron assimilation, except in the case of calcium sulfate, and the anemia was not corrected in spite of adequate iron and copper intake.

FREDEEN, Kansas City, Mo.

THE PROTEIN CONTENT OF THE ORGANS AND TISSUES AT DIFFERENT LEVELS OF PROTEIN CONSUMPTION. T. ADDIS, D. D. LEE, W. LEW and L. J. POO, J. Nutrition **19**:199 (Feb.) 1940.

Diets containing 6 per cent, 11 per cent, 16 per cent, 27 per cent and 43 per cent of protein, respectively, and almost isocaloric, containing adequate and equal minerals and vitamins, were given for eighteen days to five groups of rats, each group including 20 rats of identical body weight, 150 Gm. The protein content of various organs and tissues was determined on the eighteenth day. A sixth group of rats was killed at the start of the experiment and served as the basis, the quantities noted for these rats being subtracted from the protein values found on the eighteenth day. The diet containing 27 per cent protein produced the greatest total gain, but each organ and tissue had its own mode of reaction to an increasing supply of food protein. In other words, it was impossible to predict the effect on any part of the body from the change in the protein content of the body as a whole.

FREDEEN, Kansas City, Mo.

THE SUPPLEMENTARY VALUE OF THE BANANA IN INSTITUTION DIETS: II. CAPILLARY RESISTANCE AND REDUCED ASCORBIC ACID IN THE BLOOD PLASMA. LYDIA J. ROBERTS, MARGARET H. BROOKES, RUTH BLAIR, GERTRUDE AUSTIN and ISABEL NOBLE, J. Pediat. **15**:43 (July) 1939.

This report deals with the effect of banana supplement on the vitamin C stores of a group of boys receiving two to three bananas a day in addition to a regular institutional diet. The supplement increased the vitamin C intake from 340 to 510 international units of vitamin C (17 to 26 mg. of ascorbic acid, or 34 to 51 Sherman units). In order to determine whether the bodily stores of vitamin C were increased in the group receiving the supplement these boys were compared with a matched control group on the same diet but not receiving the supplement. The measures employed for this comparison were (1) the capillary resistance test and (2) the reduced level of ascorbic acid in the blood plasma of the boys in the two groups at the end of the study.

The differences in capillary resistance between the two groups were not large by any method of analysis, nor did they attain statistical significance, though the

level for the group receiving the supplement was consistently above that of the control group for all tests after the first one. More significant were the differences for ascorbic acid content of the blood. The boys receiving the supplement averaged 0.2 mg. per hundred cubic centimeters of plasma higher than the control group; this difference is six times the probable error and is therefore significant.

RAUH, Cincinnati.

CASES OF HYPOGLYCEMIA OF EXTRAINSULAR ORIGIN. J. GELDRICH, Orvosi hetil. **83**:809 (Aug. 19) 1939.

Geldrich reports 4 cases in which hypoglycemia became manifest in the low level of the sugar content of the blood. In the first case the cause of hypoglycemia was qualitatively and quantitatively insufficient nutrition. In the other 3 cases the condition was due to changes in the pituitary body. In the second case there was a tumor and in the third a hypoplasia of the pituitary body, while in the fourth the characteristic symptoms of pluriglandular disturbances (Simmonds' disease) were observed.

GÖTTCHE, Budapest, Hungary.

CONNECTIONS BETWEEN WATER DEFICIENCY AND METABOLISM OF CARBOHYDRATES. Ö. KERPEL-FRONIUS, Orvosi hetil. **83**:812 (Aug. 19) 1939.

Experiments on young rats showed that the rapidity with which carbohydrates are absorbed depends on the water deficiency of the tissues: The greater the deficiency, the slower the absorption. Further examinations revealed that the synthesis of glycogen in the liver cells does not show any diminution because of water deficiency. Therefore the disorder of carbohydrate metabolism in cases of dehydration is of extrahepatic origin.

GÖTTCHE, Budapest, Hungary.

IMPORTANCE OF SULPHUR IN NOURISHMENT. S. BLAZSÓ, Orvosképzés **29**:639 (July) 1939.

The metabolism of adults requires organic sulfur. From this standpoint vegetable food is not equivalent to animal food, for the sulfur content of vegetable proteins is small. The human organism, therefore, needs animal proteins. A one-sided vegetable diet is especially insufficient in cases of long and extreme exertion (sport) and after great loss of proteins (convalescence). Hence it is an old custom that convalescents are given beef tea, meat extracts and meat of young animals. Beef tea is valuable because of the high content of sulfur. Growing children need relatively more sulfur than do adults; therefore an unbalanced vegetable diet is always insufficient for children. Since the growth of infants is greater than that of children, the former need even more sulfur than the latter. Infants can best get sulfur in breast milk. The retention of sulfur from breast milk usually reaches 90 per cent, whereas the retention from artificial food is much less. This shows also that the best food for infants is breast milk. Three important sulfur compounds are known to occur in the human organism: insulin, glutathione and vitamin B_1.

GÖTTCHE, Budapest, Hungary.

Vitamins; Avitaminoses

AVITAMINOSIS WITHOUT DIETETIC DEFICIENCY. FRANK VAN DER BOGERT, Arch. Pediat. **56**:761 (Dec.) 1939.

Two cases of scurvy are reported. The condition occurred in infants that were overfed. The author feels that overfeeding may have been responsible for the occurrence of the disease despite the fact that some vitamin C–containing foods were included in the diet.

ORR, Buffalo.

THE PREVENTION OF CAROTENE ABSORPTION BY LIQUID PETROLATUM. ARTHUR C. CURTIS and ROBERT S. BALLMER, J. A. M. A. **113**:1785 (Nov. 11) 1939.

Four lubricants were administered to groups of patients on a diet high in carotene. An emulsion of 65 per cent liquid petrolatum and 10 per cent agar and one of 80 per cent petrolatum and 1 per cent agar removed considerable carotene, as was evidenced by a lowering of the blood level. Plain liquid petrolatum saturated with carotene (0.26 per cent) at room temperature (22 C.) did the same to a lesser extent, while the addition of carotene at body temperature (37 C.) prevented the removal of carotene from the blood. HEERSMA, Kalamazoo, Mich.

MINIMUM VITAMIN A AND CAROTENE REQUIREMENTS OF MAMMALIAN SPECIES. H. R. GUILBERT, C. E. HOWELL and G. H. HART, J. Nutrition **19**:91 (Jan.) 1940.

Discussing the more conspicuous symptoms of vitamin A deficiency in the horse, these investigators present data on the time required to deplete the vitamin A reserves of the horse and on the minimum requirements of this animal for vitamin A and carotene. Previously published data on the vitamin A requirement of cattle, sheep and swine are reevaluated and summarized. A table and a graph present a "summary of vitamin A and carotene requirements in relation to body weight and an illustration of requirements of a 70 kg. individual."

FREDEEN, Kansas City, Mo.

A TEST FOR THE DETERMINATION OF THE VITAMIN C STORAGE: VITAMIN C INDEX. LASLO KAJDI, JACOB LIGHT and CHARLOTTE KAJDI, J. Pediat. **15**:197 (Aug.) 1939.

The authors review the methods which have been used to determine vitamin C nutrition. The present study was undertaken in the attempt to investigate the applicability of the parenteral tolerance test to the determination of vitamin C nutrition in infants. The procedure used was as follows: After the infant had fasted a sample of blood was drawn for the determination of the level of vitamin C in the plasma. Then 200 mg. of ascorbic acid was given intramuscularly. Four hours later another blood sample was drawn. The use of the four hour interval was based on previous observations which showed that after a parenteral injection of vitamin C the plasma level rises promptly, then falls rapidly and usually by the end of four hours has reached a level which remains relatively constant during the next twenty-four hours; for after a massive parenteral dose of vitamin C, 80 per cent of the total twenty-four hour excretion takes place within the first four or five hours. This constant level occurs only in patients with stores depleted of vitamin C. In persons whose stores are better filled the level of the plasma vitamin C content obtained four hours after the injection does not persist but decreases somewhat during the following hours. This is to be expected, for well filled stores have less avidity for the vitamin and hence the constant level is obtained more slowly.

Forty-four children, 37 of whom were under 2 years of age, were studied, the parenteral tolerance test being used. Twenty-six of these patients had clinical evidence of scurvy, 7 were suspected of having a vitamin C deficiency and 11 had nothing to suggest scurvy but were hospitalized for various conditions. After the parenteral test dose at the four hour interval the final level for vitamin C in the plasma was below 0.20 mg. per hundred cubic centimeters in the scorbutic patients, between 0.20 and 0.6 mg. per hundred cubic centimeters with 1 exception, when the depletion of the vitamin C stores was serious. Values greater than 0.6 mg. per hundred cubic centimeters were obtained in all but 4 of the patients hospitalized for other conditions and in those with scurvy who had received some

treatment. In 64 out of 70 tests (91 per cent) correct information was obtained by a single determination, the four hour test.

The authors express the belief that a better means of revealing the deficient vitamin C nutrition is to use the "vitamin C index," which represents the product of the initial blood plasma value and the increase in plasma vitamin C four hours after injection, multiplied by 100. When this index was used it seemed that an index below 0.8 indicated clinical scurvy and one between 0.8 and 6 indicated very deficient reserves. In normal subjects the index is usually well above 10.

RAUH, Cincinnati.

VITAMIN-K LACK IN NORMAL AND SICK INFANTS. H. DAM, E. TAGE-HANSEN and P. PLUM, Lancet **2**:1157 (Dec. 2) 1939.

In this study the coagulation of blood was estimated by the method of Dam and Glavind, by the use of an extract of human brain.

The report consists of the case histories of 7 newborn infants and records of the examinations of the blood of 28 other infants.

In normal infants a moderate lack of vitamin K was found to develop during the first few days after birth and to disappear within a week. This results in hypoprothrombinemia, which is the cause of the slight hemorrhagic diathesis in the newborn. Its cause must be an insufficient amount of vitamin K from the intestine.

In diseases belonging to the clinical trend of icterus gravis neonatorum, anemia neonatorum and hydrops congenitus, considerable hypoprothrombinemia was demonstrated. Ingestion of vitamin K (together with bile salt) by 1 of the patients resulted in a rapid increase in prothrombin; one may presume that the hypothrombinemia in this case was due to lack of vitamin K. When a complete lack of prothrombin is seen one day after birth, other causes than insufficient absorption from the intestine must be operating.

LANGMANN, New York.

AVITAMINOSES WITH REFERENCE TO TERRAIN. GEORGES MOURIQUAND, Arch. de méd. d. enf. **42**:673 (Nov.-Dec.) 1939.

While frank illustrations of the various deficiency diseases are now noted less frequently than before the notable contributions of biochemists, there are cases of the diseases in the preclinical stage in which attenuated symptoms are exhibited and still others in which the diseases might be placed in the category of unsuspected dystrophies.

Numerous subjects living for long periods on a subminimal vitamin ration may remain in apparent good health. A slight infection or digestive disorder may suddenly affect this hidden disequilibrium and change the asymptomatic state into the symptomatic. Mouriquand asserts that the problem of unperceived dystrophies is inextricably associated with considerations of the "terrain." Study of the "terrain" reveals the influence of heredity, congenital and acquired anomalies, diet, climate and habits of life. From this point of view, the author takes up the bioclinical study of avitaminoses A, B, C and D as they are related to infantile dystrophies.

AMESSE, Denver.

DOES ULTRAVIOLET IRRADIATION OF MILK AFFECT THE VITAMIN C CONTENT? H. SCHROEDER, München. med. Wchnschr. **86**:821 (May 26) 1939.

Schroeder found that prolonged irradiation of milk destroys its ascorbic acid content. Almost 50 per cent is lost in ten minutes. With an assay of 0.19 mg. present in the beginning, there remained after ten minutes' irradiation 0.1 mg. and after thirty minutes' 0.04 mg. After an hour none could be found.

BRAHDY, Mount Vernon, N. Y.

TREATMENT OF RICKETS WITH ONE LARGE DOSE OF VITAMIN D_2. P. MÖDLINGER, Orvosi hetil. **83**:971 (Nov. 4) 1939.

Forty-three patients with rickets were treated with one large dose of vitamin D_2, 15 mg. being given to all, to 18 per os and to 23 by injection. The injection method is more exact and more trustworthy, especially when the children are vomiting; Mödlinger therefore wishes to use only the injection method in the future. The most important condition for which this treatment is indicated is rachitic tetany, for the level of calcium in the blood begins to rise within ten to twelve hours after injection of 15 mg. of vitamin D_2, and the symptoms of active tetany usually disappear in twenty-four to forty-eight hours. It is advisable to use this method on rachitic children suffering from some acute illness (such as pneumonia, whooping cough or measles), when prompt healing of rickets is desirable. One large dose seems to be effective also in prophylaxis, but the children should be controlled at least every second month. Investigations thus far have shown that the prophylactic effect of one large dose does not last longer than two months (in winter).

GÖTTCHE, Budapest, Hungary.

RESULTS OF TREATMENT OF RICKETS WITH ONE LARGE DOSE OF VITAMIN D ("STOSSTHERAPIE"). F. SZLÁVIK JR., Orvosi hetil. **83**:1030 (Dec. 9) 1939.

Vitamin D was given in one large dose to 9 patients orally and to 5 intramuscularly. The vitamin D (15 mg.) was diluted in 1 cm. of sesame oil. The treatment was used only in cases of marked rickets, and in all 14 cases a quick and decided effect was observed.

GÖTTCHE, Budapest, Hungary.

Hygiene; Growth and Nutrition; Public Health

CHEMICAL STRUCTURE AND ITS RELATION TO GROWTH AND DEVELOPMENT. F. S. HAMMETT, Am. J. Roentgenol. **43**:266 (Feb.) 1940.

This article contains statements of objects in the study of growth based on four principal aspects of living things: (1) the direction, which is the concern of genetics; (2) the substance and expression of growth, which is the concern of chemistry; (3) the state of growth, the concern of physics; (4) the form of growth, the concern of anatomy.

The functions of chemical compounds in growth are conditioned by their structure. Differentiation in cells is really chemical specialization of cell structure. The author feels that the structural nature of the molecules used in tissue growth may well condition the shape which the growing part takes. As an example, an OH group introduced into a molecule of some naturally occurring tissue component produces quite an effect as regards toxicity. Thus the chemical structure which develops during the normal course of living activity determines what the subsequent reactions shall be, which in turn determine what shall be the nature of the growth response.

SQUIRE, Chicago.

SCHOOL HEALTH IN ILLINOIS. H. H. BOYLE, S. C. HENN, J. E. CAREY and A. L. NEWCOMB, Illinois M. J. **77**:76 (Jan.) 1940.

The authors present a report of a study of the committee on school health and school health education of the Illinois section of the American Academy of Pediatrics. A questionnaire, based on suggestive material from the national committee reports as well as on the local committee's concept of an ideal program, was mailed to pediatricians and general practitioners throughout the state. About 95 per cent replied.

A summary of the answers indicates that a majority of the medium-sized communities are recognizing the value of having a physician on the Board of

Education. Most of the larger cities have full time health officers. The school nurse evidently has become acceptable to a majority of the communities. One of the outstanding lacks is in mental hygiene; there seems to be a widespread neglect of diagnosis and treatment of early manifestations of behavior difficulties in schools. Only a few communities require routine tuberculin tests of the school personnel. Few communities approach the ideal of a yearly examination of all school children.

Many of the cities, towns and rural districts of Illinois are not active along the line of school health and school health education. Only two groups of children are receiving anything approaching suitable care: those requiring immunizations and those who are crippled. Physicians have little supervision over the children needing corrective training. Less than one-half the communities reported regular dental examinations. The "summer round-up" is not being utilized to the fullest extent. There is need for extensive education of the public by physicians, nurses and allied professional groups.

BARBOUR, Peoria, Ill.

A STUDY OF THE STILLBIRTH AND NEONATAL DEATH PROBLEM: BASED ON AN ANALYSIS OF ALL OF ROCHESTER'S CASES IN 1936. HERBERT C. SOULE, New York State J. Med. **39**:1905 (Oct. 15) 1939.

The United States Bureau of Census shows that in 1936 over 137,589 infants died in the United States from causes associated with birth. Of the babies dying within the first year, 50 to 75 per cent die in the first month. A study was made of all the stillbirths and neonatal deaths in Rochester, N. Y., for the year of 1936. The infants in 83 per cent of the cases were born in eight Rochester hospitals. The hospital records were studied, and it was found that a considerable number of records were incomplete, especially in respect to antepartum care and to description of the baby and his subsequent course.

Autopsies had been performed in 43 per cent of cases, but frequently these lacked careful examination of the head for intracranial injury, and too few included microscopic examinations of the lung.

One physician made the diagnosis of patent foramen ovale in 90 per cent of his cases in which autopsy was done, and another found intrauterine asphyxia in 90 per cent. Soule questions such diagnoses and feels that pathologists should be urged to do careful and complete autopsies on these patients.

A number of charts are given, showing that Rochester has slightly lower neonatal death rates and even lower stillbirth rates than other communities.

Regarding anesthetics, Soule says that he could not "escape the conviction that where there was prematurity, pathologic presentations, or difficult delivery, the added depression of the narcosis may have been a real cause of death in some cases, especially when large doses were used."

Deaths of premature infants could be reduced by placing the children in a hospital where expert medical advice and care could be obtained. It is suggested that to reduce mortality further practitioners should be trained to recognize complications sooner in order that expert advice may be sought. Women should be educated to come earlier for antepartum care and should know that complete "obstetric amnesia" may not always be safe for the baby. A group of obstetricians, pediatricians, pathologists and health officers should meet once or twice a year in each community to study methods for reducing the death rate. Standard obstetric records should be planned; standards of procedure and hospital rules should be set up, and especially a careful review of all stillbirths and neonatal deaths should be carried out.

AIKMAN, Rochester, N. Y.

INFANT MORTALITY AND HOSPITALIZATION. M. ORTOLANI, Lattante **10**:487 (Dec.) 1939.

The author presents a plea for more children's hospitals in Italy to help lower the infant mortality rate.

HIGGINS, Boston.

Prematurity and Congenital Deformities

MORPHOLOGY AND PATHOGENESIS OF DWARFISM. W. ECKE, Fortschr. a. d. Geb. d. Röntgenstrahlen **60**:107 (Aug.) 1939.

The presence in Königsberg, Germany, of a troop of midgets provided Ecke with the rare opportunity to obtain extensive anthropometric measurements and to make roentgen examinations of 11 members of the company. In addition he procured a limited amount of information relating to genealogy and details of development; the exaggerated shyness that characterizes professional midgets precluded adequate physical examination.

The 11 midgets who submitted to investigation varied in age between 18 and 42 years and in height between 101 and 129 cm. Three pairs were composed of brother and sister. Of these, one pair came of a family consisting of a normal father and mother, 4 normal sisters, 1 normal brother and 1 dwarfed sister, in addition to the 2 midgets. The mother affirmed that the midgets' birth weights had been normal and that retarded growth did not become evident until the children were nearly 2 years of age. Dentition commenced at the usual time. The family of a second pair included 4 additional midgets and 1 normal brother. In the case of the third pair the father and mother were first cousins; 2 other children, both normal, completed the family. Concerning a fourth pair, a brother and sister, who were not examined roentgenographically and hence were not included in the series of 11, the following information was obtained: The father and mother were first cousins. The male midget was 28 years of age and measured 115 cm.; the sister was younger and somewhat smaller. Secondary sex characters had begun to make their appearance in both, the brother showing pubic hair and relatively normal genitals. The epiphyses in this midget had evidently united recently, judged by residual roentgen features. This midget showed geroderma; the sister's skin was fine. Of the remaining 5 of the 11 midgets, 1 had 2 dwarf and 1 had 3 normal siblings. No information was obtained concerning the families of the other 3. In all cases the parents and forebears were said to be normal.

All of the midgets claimed to have had normal birth weight. Retardation of development made its appearance between the second and the fifth year of life; subsequent growth had been slow, characterized by irregular spurts, and, in the majority of cases, had continued after the attainment of the twentieth year. One had increased his height by 5 cm. between the ages 32 and 42 years.

The results of extensive anthropometric measurements are supplied. Interpreted by comparison with Günther's constants for body proportions, these measurements showed that the development of the parts of the body had been harmonious, correlating well with height and poorly with chronologic age. In general, the habitus was juvenile; the head was brachycephalic and the ratio of length of forearm to length of upper part of arm consistently high. All were overweight in varying degree although muscularly well developed. The distribution of the subcutaneous fat bespoke a juvenile stage of physical development; the same was true of the countenance. The quality of the skin was more appropriate to the chronologic age than to the state of physical maturity. The hair of the body and face was soft, sometimes silky. In no case had change of voice occurred. In the 2 instances in which examination was permitted, the penis and scrotum were those of boys of corresponding size; the external genitals were half-hidden in the pudendal fat, and the testes could not be felt. A cooperative subject reported that the gonads of the other 7 males were "noch im Leib" (still in the body). In no case could the thyroid gland be felt. Intelligence was normal. The midgets were unusually reliable in keeping promises. Aside from a certain amount of compensatory braggadocio and pompousness, the emotional life did not appear remarkable. Four subjects had a normal white blood cell count with a slight relative lymphocytosis. Five showed normal electrocardiographic tracings.

Roentgen examination revealed measurable enlargement of the projection of the sella turcica in 6 cases out of 11. In every case the development of the

skeleton was conspicuously retarded. The specific points of immaturity were: ununited epiphyses, thin vertebral bodies with wide intervertebral disks, a juvenile pelvic outline, pseudoepiphyses and supernumerary epiphyses. The average age of the 11 subjects was 28 years; the average skeletal development corresponded to 12 years. [Graphic analysis shows a high positive correlation between chronologic and skeletal ages with only a moderate error of prediction.—Abstracter.] A number of unfamiliar findings are reported for the first time: (1) the frequent occurrence of brachymesophalangia of the fifth finger, a common feature in mongolism; (2) marked retardation of the development of the paranasal accessory sinuses, the average degree of maturity equaling 7 years; (3) the presence in 8 of the 11 subjects of pathologic changes in the hip joint akin to Perthes' disease or punctate epiphysial dysgenesis in various stages of progression and reparation. In several instances Köhler's disease of the tarsal scaphoid was encountered; aseptic epiphysial necrosis in the region of the elbow was noted twice.

Ecke concludes that the type of hereditary dwarfism exhibited by these midgets is mediated by the hypophysis, citing Koch's autopsy, which was interpreted by Berblinger in the same sense. He also calls attention to Eidmann's observation on dwarfism in frogs, those of Smith and McDowell on hereditary dwarfism in mice and those of Lambert and Scuichetti in similarly stigmatized rats. Reference is made to the Hanhart group of dwarfs, whose dwarfism was formerly ascribed to diencephalic causes but was probably of pituitary origin. Attention is called to the not infrequent occurrence of skeletal anomalies in families which beget dwarfs.

Retarded development of the paranasal accessory sinuses is a characteristic feature of the type of dwarfism represented by these midgets. Previous assertions to the contrary are erroneous inasmuch as the standards of comparisons were inaccurate.

Aseptic necrosis of the epiphyses is a comparatively rare finding in epiphysial dwarfism, although it has been observed by a few earlier authors. The lesion apparently depends on a disturbance of the function of the glands of internal secretion; that it is not to be regarded as a coordinated anomaly of development is demonstrated by the report of Engelbach and Schäfer (it can be cured by organotherapy); also, by the parallelism between the degree of development and the severity of the lesion in the patients under discussion; finally, by the frequency of comparable lesions in congenital hypothyroidism. Similar lesions were produced by Schäfer in salamanders.

The bibliography is useful. McCUNE, New York.

Newborn

RELATION OF THE VOLUME OF PULMONARY CIRCULATION TO RESPIRATION AT BIRTH. S. ABEL and W. F. WINDLE, Anat. Rec. **75**:451 (Dec.) 1939.

There have been divergent opinions as to the amount of blood coursing through the lungs prior to the onset of respiration and after. Some believe that the change is traumatic and others that it is gradual. The authors estimated the iron content of lungs from fetal kittens and guinea pigs and from those living for one to twenty-four hours. From these estimates and from estimations of hemoglobin, there is no significant difference. It appears, then, that the circulation is well established in the lung during late fetal life. SNELLING, Toronto, Canada.

CEREBRAL MANIFESTATIONS IN THE NEWBORN. A. LEVINSON, Arch. Pediat. **56**:210 (April) 1939.

Until recently the only cerebral condition in the newborn that attracted attention in medical literature was cerebral hemorrhage, which was thought to manifest itself in the neonatal period mainly by convulsions and to be followed later by

spastic paralysis. Recently it has been determined that other conditions of the newborn may cause cerebral phenomena. These cerebral conditions may vary in type and degree, as is shown in the following list of symptoms:

Tremors	Apathy
Convulsions	Somnolence
Moaning	Weak cry
Bulging fontanel	Fleeting cyanosis
Rigidity	Vomiting
Paralysis	

The treatment varies with the cause, but certain principles should govern the management of all cerebral manifestations and their prevention. They are:

Rest	Intramuscular injections of blood for cerebral hemorrhage
Maintenance of body heat	Calcium for tetany
Oxygen for cyanosis	Carbohydrates in hypoglycemia
Small feedings	Removal of any focus of infection when possible
Hypertonic dextrose, sedatives, spinal puncture for convulsions	

Since the treatment may vary with the cause, each condition must be considered separately. The causes of cerebral manifestations in the newborn are:

Concussion of the brain	Acute general infections
Cyanosis	Meningitis and encephalitis
Tetany	Syphilis
Hypoglycemia	Nuclear (Kern) icterus
Cerebral hemorrhage	Tetanus neonatorum
Cerebral agenesis	

The incidence of cerebral hemorrhage in 2,633 full term and prematurely born infants at Michael Reese Hospital may be stated as follows:

	Full Term (2 Yr. Period)	Premature (7 Yr. Period)
Infants	2,633	1,527
Cerebral hemorrhage	12	292
Percentage of total	0.45	19.1

The symptoms of cerebral hemorrhage are of two types: irritative and somnolent; a combination of the two is possible.

Those indicative of irritation are restlessness, a high-pitched cephalic cry, moaning and a pained expression. Spasticity may come on immediately or after a few days or weeks. Bulging of the anterior fontanel is frequent with this type of hemorrhage. Occasionally there is rigidity of the neck and even opisthotonos.

The somnolent symptoms are apathy, subnormal temperature, difficulty in swallowing, fleeting cyanosis and usually a depressed fontanel. The infants with these symptoms refuse food or take very little and suffer as a result from dehydration. The skin is dusky red, a condition which may persist for some time. Many infants with cerebral hemorrhage have atelectasis, which may produce cyanosis.

The prevention of cerebral manifestations is more easily spoken of than accomplished. Sometimes, no matter what is done, cerebral irritation or hemorrhage will occur. The author suggests the following preventive measures:

1. Prevention of prematurity, particularly that due to syphilis and eclampsia. A Wassermann or Kahn test should be made on all pregnant women, and if the results are positive, the future mother should be subjected to a rigid course of antisyphilitic treatment. Repeated determinations of the blood pressure should be made and treatment given against eclampsia.

2. Judicial use of forceps. Avoid the use of forceps when possible but apply them if labor becomes prolonged.

3. Strict asepsis, particularly as to the umbilicus.

4. Limitation of prelacteal feeding.

5. As little as possible of disturbance of the newborn.

ORR, Buffalo.

SALMONELLA INFECTION OF THE NEWBORN: ITS DIFFERENTIATION FROM EPIDEMIC DIARRHEA AND OTHER PRIMARY ENTERIC DISORDERS OF THE NEWBORN. H. ABRAMSON, S. FRANT and C. OLDENBUSCH, M. Clin. North America **23**:591 (May) 1939.

The genus Salmonella comprises a large number of strains which are intermediate between the colon and the dysentery group, having certain biologic and serologic characteristics in common with both. In man, an infection with organisms of this group may result in brief acute gastroenteritis, in prolonged typhoid-like disease or in generalized sepsis. "Asymptomatic," or "silent," infection may be discovered by examination of the stools of exposed patients. The role of the latter as "carriers" is important when the disease occurs in epidemic form.

The disease in infants and older children is characterized by an abrupt onset, with symptoms referable to the central nervous system, such as headache, convulsions and stupor. Gastrointestinal symptoms (nausea, vomiting and diarrhea) appear early. Only rarely has the disease been reported as occurring in newborn infants. The authors report a small epidemic involving infants in a nursery of a general hospital, 4 of whom died. From the stools an organism of the Salmonella group was recovered; a similar organism was found in the stool of a nurse on duty in the nursery. In cases in which such infection is suspected the stool should be examined early, since the organisms disappear rapidly, even though pus and blood remain. Salmonella infections in newborn infants are characterized by abrupt onset, high fever, prostration, convulsions and widespread involvement of the central nervous system and of the respiratory and the skeletal systems, resulting in meningitis, pneumonia and other local lesions. Organisms of the Salmonella group may be found in the stools of newborn infants, in the blood, in the urine and in the exudates. By contrast, the onset of epidemic diarrhea of the newborn is slower and less violent. The fever is low, and convulsions do not occur. The stools are yellow and watery and contain no serous organism. Widespread sepsis rarely occurs.

EUGENE H. SMITH, Ogden, Utah.

THE ASPHYXIATED INFANT. H. A. CUNNINGHAM and A. B. SCHWARTZ, Wisconsin M. J. **38**:632 (Aug.) 1939.

Asphyxia is a common emergency in the newborn. Important in determining the likelihood of asphyxia are the kind of labor, the type of narcotics or anesthetics used before and during delivery and the kind of baby (premature or full term). Regardless of cause, the hazards are, first, those of obstruction and, second, those due to anoxemia without obstruction. Great care should be taken to see that the method of therapy is not injurious.

Cruickshank's work showed that 20 per cent of 800 infants who died had gross intracranial hemorrhage and that many more had congestion and edema. These findings are largely ignored in present practices of resuscitation, with the result that asphyxia is aggravated.

Practical and easily available methods of combating asphyxia should be used. Cleansing the air passages, starting respiration and administering oxygen with carbon dioxide are the chief needs, then carefully supervised nursing care, with warmth and no unnecessary handling. Feedings should be given artificially with a medicine dropper, and oxygen should be administered for ten minutes, three times a day.

JANNEY, Wauwatosa, Wis.

NOTES ON THE SURGERY OF THE NEWBORN: THE FETAL ATRESIAS. I. AIRD, Edinburgh M. J. **46**:174 (Nov.) 1939.

Most textbooks of embryology do not mention the occurrence of any congenital anomaly, nor has a theory been elaborated which covers all the locations and which applies to and explains both obliterative abnormalities and the common sites of congenital deformities, such as the face, the middle of the duodenum and the anus. Aird believes that atresia is the result of fetal overstretching, which should explain even the complete absence of the rectum.

He discusses the surgical treatment. The failure of all efforts to save the life of the infant born with esophageal atresia is due to aspiration of food, for, even after gastrotomy, food ascends the lower part of the esophagus and enters the trachea. It would be safer in such attempts at surgical relief to occlude the cardia by stitching through the lumen of the stomach.

Atresia of the duodenum calls for lateral anastomosis, which can be facilitated by inserting temporarily a catheter through an incision into the lumen of the distal part of the bowel. This prevents distortion and obliteration of the lumen below the obstruction while suturing is done. NEFF, Kansas City, Mo.

Acute Contagious Diseases

ATTEMPTS TO ISOLATE POLIOMYELITIS VIRUS WITH THE STOOLS OF HUMAN BEINGS AND THE EXPERIMENTAL ANIMAL. JOHN A. TOOMEY, Arch. Pediat. **56**:693 (Nov.) 1939.

The author, as well as others, has demonstrated that the virus of anterior poliomyelitis can be recovered from the stools of human beings ill with the disease. It has been proved by others that the virus is present in sewage in areas where the disease is prevalent. These results tend to support the belief that the virus of anterior poliomyelitis enters the human system by way of the gastrointestinal tract and do not support the theory that the nasal passage is even an occasional port of entry of the disease, let alone the sole one. ORR, Buffalo.

IMMUNIZATIONS. R. C. FARRIER, Illinois M. J. **77**:63 (Jan.) 1940.

Farrier discusses the antitoxins and vaccines that have to do with immunizing against typhoid fever, diphtheria, whooping cough, scarlet fever and smallpox.

BARBOUR, Peoria, Ill.

AN EPIDEMIC OF POLIOMYELITIS IN WHICH BULBAR PARALYSIS OCCURRED WITH UNUSUAL FREQUENCY. ERNEST L. STEBBINS, EDWARD E. GILLICK and HOLLIS E. INGRAHAM, J. A. M. A. **113**:1559 (Oct. 21) 1939.

A high incidence of poliomyelitis occurred in Niagara Falls, N. Y., during the summer of 1938, while surrounding counties reported few cases. Among the 20 patients bulbar involvement occurred in 13, of whom 12 died. There was no definite evidence of a common source and no reason was apparent for the high incidence of bulbar involvement. HEERSMA, Kalamazoo, Mich.

DIFFICULTIES ENCOUNTERED IN A TEST FOR STANDARDIZATION OF TOXIN USED AGAINST SCARLET FEVER. B. S. KOLCHIN, J. Lab. & Clin. Med. **25**:762 (April) 1940.

Irregularities in skin reactions have caused difficulties in the standardization of scarlet fever toxin preparations. READING, Galveston, Texas.

II. Treatment of Scarlet Fever with Specific Antitoxins of Low Protein Content. John A. Toomey and E. Robbins Kimball Jr., J. Pediat. **15**:238 (Aug.) 1939.

This report deals with the results obtained in 500 cases of scarlet fever with the use of a new type of concentrated scarlet fever antitoxin. Serum reactions were few and mild; the temperature fell rapidly, complications were probably decreased in number and severity and the rash disappeared quickly.

Rauh, Cincinnati.

Can Infantile Paralysis Be Spread by Bathing in Sewage-Polluted Waters? Samuel M. Ellsworth, New England J. Med. **222**:55 (Jan. 11) 1940.

Prior to 1912 it had been demonstrated that the virus of infantile paralysis could be recovered from the mucosa of the intestinal tract and from the feces.

Lovett and Richardson, as far back as 1911, reported that in 419 cases observed from 1908 to 1910, 105 patients, or slightly more than 25 per cent, had swum, waded or paddled in more or less contaminated water just prior to the attack. However, these authors also called attention to 457 cases during the same period, in 34 per cent of which the patients reported precedent accidents, overexertion or falls.

Trask, Vignec and Paul have recently reported on the recovery of the virus from the stools of an infant after abortive poliomyelitis. Emulsions prepared from the stools on the second, the fourteenth and the twenty-fifth day after the onset of the disease were used to inoculate monkeys. In each case paralysis developed seven days after inoculation. As evidence of the resistance of the virus, one of the samples of the stool was kept under refrigeration for ten weeks, and the virus remained viable.

Another recent discovery which may have a bearing on the theory of spread of infection by bathing is reported by Howe and Bodian. They describe the infection of monkeys following the dropping of the virus of poliomyelitis into the conjunctival sac.

Gengenbach, Denver.

Fatal Prodromal Measles. Seymour L. Homrighouse and Thistle M. McKee, New York State J. Med. **39**:1934 (Oct. 15) 1939.

A boy 21 months of age was exposed to measles, and two days later intermittent cough and dyspnea developed. For the next three days he had no fever but had some dyspnea, which was worse at night. A roentgenogram of the chest was taken to rule out the possibility of a foreign body. Attacks of coughing continued, and on the fourteenth day after the first appearance of symptoms the patient had severe dyspnea. Bronchoscopic examination revealed decided edema of the larynx. The dyspnea became more marked, and tracheotomy was necessary. The child died several hours later.

Autopsy revealed many giant cells in the tonsils, in the laryngeal and tracheal mucosa, in the thymus and in the spleen. In view of the history of exposure to measles and the finding of the giant cells, it appears likely that measles occurred as a terminal complication and was not the primary cause of death.

Aikman, Rochester, N. Y.

The Anatomical Distribution and Character of the Lesions of Poliomyelitis, with Special Reference to the Type of Cell Affected and to Portal of Entry of the Virus. C. Swan, Australian J. Exper. Biol. & M. Sc. **17**:345 (Dec.) 1939.

Swan examined the central nervous systems of 8 patients with poliomyelitis by routine neurohistologic methods. There was no evidence of an absolute specificity

of the virus for cells of the motor type in the cranial part of the nervous system, except perhaps in the cerebral cortex and the cerebellum. Neither was there any in the spinal cord, for though the chief changes were in the anterior horn cells, occasional cells of Clarke's column and of the posterior root ganglions were also affected. It must be said, however, that cells of the motor type are more often and more severely affected than any others. In 4 cases in which they were examined the olfactory bulbs were free from pathologic changes. Other observers having noted the absence of changes in the olfactory bulbs, Swan believes that infection by the virus of poliomyelitis by the olfactory route is either less common than was formerly thought or is not commonly fatal. The pontile region was severely affected in 5 cases and moderately affected in 1. The most intense changes were seen in the tissues forming the floor of the fourth ventricle. This fact prompted consideration of the medial longitudinal bundle (which extends through the whole length of the brain stem and below is continuous with the anterior intersegmental tract of the spinal cord) as an important path for the spread of the pathologic process.

GONCE, Madison, Wis.

THE IMMUNITY FOLLOWING INTRACUTANEOUS AND SUBCUTANEOUS VACCINATION WITH ELEMENTARY BODY SUSPENSIONS OF VACCINIA. R. G. HENDERSON and D. MCCLEAN, J. Hyg. **39**:680 (Nov.) 1939.

Intracutaneous and subcutaneous vaccinations with a bacteria-free elementary body suspension prepared directly from vaccine pulp were done on 131 adults and 197 children. Immunity resulting from the intracutaneous method was tested by revaccination by scarification with vaccine lymph after a six weeks interval or more. A control group was vaccinated by scarification with the same elementary body suspension and similarly tested for immunity. There seemed a definite correlation between the appearance of a typical epidermal vesicle after the primary vaccination and the subsequent development of immunity. Among 75 in whom vesicles developed, 72 were completely refractory to revaccination and 2 of the remaining 3 had modified lesions on revaccination. Among 89 subjects in whom vesicles did not develop, 58 had typical vaccinial reactions on revaccination. While immunity to smallpox is general and humoral, it may be that proliferation of the vaccine virus in the epidermis is in some way necessary to insure the development of firm immunity in man.

JANNEY, Wauwatosa, Wis.

ACUTE ANTERIOR POLIOMYELITIS: A REVIEW OF 250 CASES IN SYDNEY DURING THE 1937-1938 EPIDEMIC. D. G. HAMILTON, M. J. Australia **1**:148 (Feb. 3) 1940.

Two hundred and fifty cases of acute anterior poliomyelitis occurring in Sydney, Australia, in the epidemic of 1937 and 1938 are discussed with respect to symptoms, signs, changes in the cerebrospinal fluid, treatment and diagnosis.

GONCE, Madison, Wis.

AN EXAMINATION OF THE OLFACTORY BULBS IN FATAL CASES OF POLIOMYELITIS DURING THE VICTORIAN EPIDEMIC OF 1937-1938. E. G. ROBERTSON, M. J. Australia **1**:156 (Feb. 3) 1940.

A study of 20 olfactory bulbs, 9 pairs and 2 single specimens, from 11 patients who had died of poliomyelitis afforded no definite evidence for or against invasion of the nervous system by the olfactory pathway. In 1 olfactory bulb from a series of 9 patients with early pharyngeal or respiratory palsy or both, inflammatory changes were noted. In 3 olfactory bulbs from 2 patients with paralysis of the skeletal muscles and without pharyngeal paralysis no inflammatory changes were noted. The accumulated evidence suggests that the virus may reach the

central nervous system by pathways other than the olfactory and that when bulbar palsy is an early manifestation the afferent pathway is probably along the glossopharyngeal nerves from the pharyngeal and tonsillar regions.

GONCE, Madison, Wis.

POOLED ADULT SERUM IN THE PROPHYLAXIS OF MEASLES. H. W. BULL, M. J. Australia **1**:228 (Feb. 17) 1940.

Pooled adult serum aged either three years or six to nine months was given to exposed children before the fourth day after the appearance of the rash in the infecting patient. The serum that had been stored for nearly three years seemed quite as effective as that collected six to nine months before use. Of 258 children treated, 67 escaped the disease; 151 had it in the attenuated form, with no prodromal sickness and no complications of any kind; 37 had moderate attacks, and only 3 had severe attacks, 1 with slight bronchopneumonia. Over 10 per cent of the patients among untreated children under 6 years of age in the rest of the population had severe complications (usually bronchopneumonia requiring hospital treatment), and 2 died.

GONCE, Madison, Wis.

ENCEPHALITIS FOLLOWING MEASLES. D. PAULIAN and CARDAS, Rev. neurol. **71**:457 (April) 1939.

A girl of 6 years had measles. Six days later her right arm became weak, and her gait became unsteady. Her speech was unintelligible. She was very irritable. Within two days her speech became clearer, although it was still nasal. The left pupil was larger than the right. Voluntary movements of the arms and legs were possible, but on the right they were poorly performed. The cerebrospinal fluid was essentially normal. Recovery was complete within ten days.

DAFFINEE, Boston.

PERLÈCHE (FAULECHEN, ANGULI FOETIDI) AS A COMPLICATION OF SCARLET FEVER. A. HOTTINGER, Ann. pædiat. **155**:9 (April) 1940.

During the 1939 epidemic of scarlet fever in Basel, Switzerland, a very mild epidemic of slight and very slight perlèche was observed, frequently as a true complication. This disease occurred more often than all the other complications. At the beginning of the epidemic it was observed in 43 per cent of all the patients; it became scantier during the course of the epidemic but occurred still in 25 per cent of all the patients with scarlatina.

The regularity of its occurrence, the course, the time needed for healing, the scar formation, the relapse of the perlèche showed, during this epidemic, a certain parallelism with the general course of the primary disease, so that clinical conclusions about the reaction of the organism to the infection could be drawn from observation of the perlèche.

Perlèche and the scar formation were of great importance for the late diagnosis of abortive or undiagnosed scarlet fever.

The occurrence of hemolytic streptococci in the majority of cases proves conclusively that the perlèche was specific for scarlatina during this epidemic.

FROM AUTHOR'S SUMMARY.

VITAMIN C IN TREATMENT OF ACUTE INFECTIOUS DISEASES. F. SZIRMAI, Orvosi hetil. **83**:961 (Oct. 28) 1939.

To patients with diphtheria, typhoid fever and pneumonia, Szirmai gave vitamin C in large doses and found that it seemed to lower the mortality rate of malignant diphtheria (150 to 300 mg. of ascorbic acid was given daily in injec-

tions and 50 to 100 mg. by mouth). In cases of typhoid fever, all the patients received 50 to 300 mg. of vitamin C as long as they had fever. Since using this treatment Szirmai had not encountered a single instance of intestinal bleeding. In cases of pneumonia vitamin C seemed less effective.

GÖTTCHE, Budapest, Hungary.

Acute Infectious Diseases

THE PROBLEM OF "RHEUMATISM" AND ARTHRITIS: REVIEW OF AMERICAN AND ENGLISH LITERATURE FOR 1938 (SIXTH RHEUMATISM REVIEW). PART I. P. S. HENCH, W. BAUER, M. H. DAWSON, F. HALL, W. P. HOLBROOK, J. A. KEY and C. MCEWEN, Ann. Int. Med. **13**:1655 (March) 1940.

This sixth review contains, in 83 pages, a complete discussion of the various types of rheumatism and arthritis encountered. In general, it follows the outline presented in former reviews.

READING, Galveston, Texas.

RHEUMATIC FEVER IN CHILDREN: ETIOLOGY. GEORGE L. DRENNAN, Illinois M. J. **76**:524 (Dec.) 1939.

Although it is generally accepted that rheumatic fever is bacterial in origin, no micro-organism has been proved to be responsible. The streptococci, viruses, allergy and vitamin C deficiency have been considered as etiologic factors. Unfavorable environmental conditions, foci of infection, seasonal and geographic distribution and age at onset seem to have their place as contributing factors.

BARBOUR, Peoria, Ill.

SIGNS AND SYMPTOMS OF RHEUMATIC FEVER. KING WOODWARD, Illinois M. J. **76**:526 (Dec.) 1939.

Rheumatic fever in childhood is a systemic infection with manifold signs and symptoms of greatly varying degrees of severity and duration, which differ markedly from those of the rheumatic fever seen in adult life.

BARBOUR, Peoria, Ill.

TREATMENT OF RHEUMATIC FEVER IN CHILDREN. H. WILLIAM ELGHAMMER, Illinois M. J. **76**:527 (Dec.) 1939.

Treatment directed against the systemic phase and the local manifestations of rheumatic fever is considered. The many measures to be considered in the prophylaxis of the infection are discussed. The familial tendency is pointed out. Among the active therapeutic measures rest, a well balanced diet, the use of salicylates and protection against recurrences are discussed.

BARBOUR, Peoria, Ill.

PATHOLOGY OF RHEUMATIC FEVER. STANLEY GIBSON, Illinois M. J. **76**:530 (Dec.) 1939.

Rheumatic fever is an infectious disease which manifests itself chiefly by symptoms and signs referable to the joints, the central nervous system and the heart. The subcutaneous tissues, blood vessels, lungs and muscles share in the rheumatic invasion.

The two prominent features which characterize the minute changes in tissue associated with rheumatic fevers are exudation and proliferation. These changes are found in the joint cavities, the pericardial sac, the pleural cavity, the heart muscle and the subcutaneous nodules.

Of 1,068 patients at the Children's Memorial Hospital and St. Luke's Hospital (Chicago), 459 had chorea, 650 had polyarthritis and 627 had rheumatic heart disease. Of the 459 children with chorea, 208 had no other evidence of rheumatism. Polyarthritis occurred in 164 and heart disease in 176. Of the 650 children who suffered from polyarthritis, 157 had polyarthritis alone, 164 had chorea and 420 had signs of heart disease. Of the 627 patients with rheumatic heart disease 97 had no history either of pains in the joints or of chorea. Present figures reveal that almost 60 per cent of rheumatic children have cardiac damage. These facts should emphasize the gravity of rheumatic infection in childhood.

BARBOUR, Peoria, Ill.

THE CLINICAL IMPORTANCE OF INFECTION OF THE RESPIRATORY TRACT IN RHEUMATIC FEVER. T. DUCKETT JONES and JOHN R. MOTE, J. A. M. A. **113**:898 (Sept. 2) 1939.

Seven hundred and forty-nine patients with rheumatic fever were studied throughout one year in an attempt to correlate rheumatic infections and recurrences with preceding colds and sore throats. Many of the observations were checked by cultures and by determinations of serum antibodies.

More than half of the first attacks of rheumatic fever were associated with infections of the upper respiratory tract. In the others infection due to hemolytic streptococci seemed to be present, as evidenced by serologic studies.

During the inactive stage of the disease recurrences followed one half of the sore throats and one third of the colds. The longer the interval the less chance there was of recurrence. While one third of the recurrences seemed to be preceded by no disease of the upper respiratory tract, studies of the blood again revealed hemolytic streptococci.

HEERSMA, Kalamazoo, Mich.

SULFAPYRIDINE IN THE TREATMENT OF STAPHYLOCOCCUS AUREUS BACTEREMIA. SAMUEL L. GOLDBERG and ALLAN SACHS, J. A. M. A. **113**:1639 (Oct. 28) 1939.

Two children, 28 months and 11 years old respectively, who had both septicemia due to Staphylococcus aureus and osteomyelitis, were treated with sulfapyridine. Although culture of the blood gave negative results and clinical improvement ensued, drainage of the osseous condition was carried out. Since the mortality of this condition is high, even 2 cures suggest the value of the treatment.

HEERSMA, Kalamazoo, Mich.

ACUTE COCCIDIOIDOMYCOSIS WITH ERYTHEMA NODOSUM IN CHILDREN. HAROLD K. FABER, CHARLES E. SMITH and ERNEST C. DICKSON, J. Pediat. **15**:163 (Aug.) 1939.

The authors describe an acute febrile disease caused by the fungus Coccidioides immitis. The disease is largely confined to the San Joaquin Valley in California, though sporadic cases have been observed in Arizona. Owing to modern conditions of travel and of migrations of labor, the disease may be encountered anywhere in the country. It is characterized by initial systemic symptoms similar to those of influenza, involving both the upper and the lower portions of the respiratory tract and commonly followed by erythema nodosum. The diagnosis is usually established by a positive coccidioidin dermal reaction and the finding of C. immitis in the sputum. This disease is common among children. The prognosis, in contrast to that of coccidioidal granuloma, which is caused by the same organism, is favorable.

RAUH, Cincinnati.

CHARACTERISTICS OF FUNGUS DISEASES. ARTHUR T. HENRICI, J. Bact. **39**:113 (Feb.) 1940.

The outstanding characteristic of the fungous diseases is their marked tendency to give rise to hypersensitivity of a type best designated as the allergy of infection, distinct from other categories of hypersensitivity. The author believes "that the other characteristics of the mycoses, age and occupational incidence, course and pathology, are strongly colored by or dependent upon this allergy. This characteristic distinguishes the fungous diseases from most of the other microbic diseases, but closely relates them to tuberculosis, and in some aspects to leprosy, syphilis, glanders, tularemia, and lymphogranuloma inguinale. These diseases present a common problem in immunology more or less peculiar to themselves." The author suggests "that this characteristic is determined by the ability of the pathogenic fungi and related microbes to produce peculiar antigen-like substances having specific properties not common to all antigens, and that the deep seated mycoses are caused by occasional species of saprophytic fungi which, evolving in restricted areas, have by chance acquired the ability to synthesize such substances."

STOESSER, Minneapolis.

A COMPARATIVE STUDY OF RICKETTSIAL STRAINS FROM AN INFECTION OF TICKS IN MONTANA (UNITED STATES OF AMERICA) AND FROM "Q" FEVER. F. M. BURNET and M. FREEMAN, M. J. Australia **2**:887 (Dec. 16) 1939.

The authors found that the rickettsia isolated by Davis and Cox from ticks in Montana and by Dyer from human beings with laboratory infection are immunologically indistinguishable from the rickettsia of Australian "Q" fever.

The American strain and the Australian strain are pathogenic for guinea pigs, mice and two species of monkey. The American strain is of greater virulence for all three species and if a large enough dose is administered produces fatal infection in guinea pigs. Both types should be included in the same species of rickettsia.

GONCE, Madison, Wis.

THE COMMON DOG TICK Haemaphysalis Leachi AS A VECTOR OF TICK TYPHUS. J. GEAR and B. DE MEILLON, South African M. J. **13**:815 (Dec. 23) 1939.

The successful transmission of the virus of tick typhus by Haemaphysalis leachi, the common dog tick, to guinea pigs while feeding is described. The ticks were obtained from a dog owned by a patient who suffered from a severe attack of tick bite fever, and it is assumed that the patient contracted the illness by contact with the tick-infested dog, either by deticking it or by allowing the dog to sleep in the owner's bed.

GONCE, Madison, Wis.

THE COURSE OF OTITIS MEDIA COMPLICATING BACILLARY DYSENTERY IN INFANCY (PRELIMINARY COMMUNICATION). I. S. NEDELSON, Vrach. delo **21**:243, 1939.

A study of the clinical picture of otitis media in infants with bacillary dysentery is presented and illustrated by reports of 3 cases. Among 183 patients under 5 years of age with bacillary dysentery, otitis was observed in 56, or 30.6 per cent. It is pointed out that the younger the child the greater the incidence of otitis. Thus, otitis media occurred in 37.5 per cent of children under 1 year of age, as compared with 7.1 per cent of those from 3 to 5 years. Otitis media complicating dysentery has been found by the author to occur in the later stages of the disease. It is stated that the symptom complex of otitis media in cases of bacillary dysentery is not clearly defined. The local signs are seldom marked, and purulent drainage fluid is rarely obtained on myringotomy. The condition should be suspected when a sudden aggravation of the general condition is observed. In all 3 patients reported on by the author a marked improvement in the general condition followed myringotomy.

BODER, Los Angeles.

Chronic Infectious Diseases

INTERSTITIAL KERATITIS IN PATIENTS WITH NEUROSYPHILIS OF CONGENITAL ORIGIN, WITH A DISCUSSION OF FEVER AS A PRECIPITATING FACTOR OF KERATITIS IN THE PARETIC VARIETY. I. KOPP and H. C. SOLOMON, Am. J. Syph., Gonor. & Ven. Dis. **23**:751 (Nov.) 1939.

"Interstitial keratitis is a relatively rare concomitant of juvenile paresis or of congenital neurosyphilis, in contrast to its relative frequency in congenital syphilis. The literature has but few references to the subject of interstitial keratitis in juvenile paresis." A few brief statistical statements follow indicating the incidence of this condition. "In our own series of 9 cases of juvenile neurosyphilis (other than the paretic type), in only 2 was there any evidence of interstitial keratitis occurring prior to treatment." In contradistinction to this the incidence of interstitial keratitis in congenital syphilis is stated.

Protocols on 7 cases are then supplied. The discussion follows, indicating the incidence of certain syphilitic complications, notably keratitis after or during treatment with malaria, drugs, artificial fever and other means. A type of keratitis has been noted as an accompaniment of malaria but it is not in the true sense of the word interstitial or parenchymatous keratitis. It is acute and occurs at the height of the fever. The condition is thoroughly discussed, the arguments pro and con being set forth, with the conclusion that interstitial keratitis is a very unusual manifestation of acquired syphilis in contrast to its frequency in congenital syphilis and is not to be expected in the person with dementia paralytica whose syphilis has been acquired.

ROYSTER, University, Va.

CHANGES IN THE LONG BONES OF NEWBORN INFANTS FOLLOWING THE ADMINISTRATION OF BISMUTH DURING PREGNANCY. J. WHITRIDGE JR., Am. J. Syph., Gonor. & Ven. Dis. **24**:223 (March) 1940.

Roentgenologic studies were made of long bones of newly born infants whose mothers had received intramuscular injections of bismuth compounds during pregnancy. It has been felt that the changes shown were those of healed syphilitic osteochondritis. Tests were made on a series of 12 women in the last trimester of pregnancy who had had two negative serologic tests for syphilis during pregnancy and no history of syphilis or of treatment for it. The same injections of a bismuth preparation were given to them as to syphilitic mothers, and the conclusion of the author is that the changes were produced by bismuth and not by healing of syphilitic osteochondritis and that the alterations were independent of the total amount of bismuth given.

ROYSTER, University, Va.

ANALYSIS OF THE TUBERCLE BACILLUS AND ITS NATURAL PRODUCTS BY IMMUNE, ALLERGIC, AND ANAPHYLACTIC TESTS. H. J. CORPER, J. Infect. Dis. **66**:23 (Jan.-Feb.) 1940.

Maximum growth of human tubercle bacilli occurs within two to three months, after which tuberculoprotein is liberated into the medium.

The bacillary body sensitizes primarily to tuberculoallergy and immunizes against virulent infections; the tuberculoprotein sensitizes to anaphylaxis and provokes anaphylactic shock and allergic intoxication but does not sensitize to allergy or immunize against virulent infections.

Tuberculoanaphylaxis, tuberculoallergy and tuberculoimmunity show characteristics distinctive enough to warrant the conclusion that they are separate and unrelated biologic phenomena.

TOOMEY, Cleveland.

DIAGNOSIS OF CONGENITAL SYPHILIS: PATHOGNOMONIC CRITERIA. WILLIAM C. BLACK, J. Pediat. **14**:761 (June) 1939.

Black reviews and evaluates existing means of diagnosis of congenital syphilis and formulates an outline of pathognomonic criteria. A thorough discussion of

bacteriologic, serologic and roentgen osseous examinations is included. "Pathognomonic evidence of the presence of syphilis in living infants and children," he states, "is seldom afforded by the results of physical examination but is to be found in the results of properly interpreted dark-field, serologic and roentgenologic examinations." Three tables accompany this paper. Table 1 presents a suggested chronologic order of procedure for the recognition of syphilis in young infants. Tables 2 and 3 offer tentative criteria for establishing the presence or absence of congenital syphilis in infants and children.

RAUH, Cincinnati.

COMPARISON OF THE VOLLMER TUBERCULIN PATCH TEST WITH PURIFIED PROTEIN DERIVATIVE: RESULTS OF TESTS ON 880 RURAL SCHOOL CHILDREN IN ST. MARY'S COUNTY, MARYLAND. EUGENE C. PECK and MYRON E. WEGMAN, J. Pediat. **15**:219 (Aug.) 1939.

"Eight hundred and eighty tuberculin tests were done on school children comparing the Vollmer patch test with the PPD intradermal test. The patch was found positive in only 30 per cent of the cases positive to PPD I or II. It is believed that this is sufficient evidence that a negative patch test does not by any means eliminate the possibility of a positive reaction to tuberculin and that the patch test alone is unsuitable as a screening method for finding the tuberculin reactors in a school population."

AUTHORS' SUMMARY AND CONCLUSIONS.

EXPULSION OF PNEUMOLITHS IN A CASE OF PRIMARY PULMONARY TUBERCULOSIS. L. DE CASTRO FREIRE and A. SALDANHA, Presse méd. **47**:1647 (Dec. 19) 1939.

Castro Freire had followed the child under discussion from the age of 3 months. No evidence of tuberculosis was found until the age of 3 years, when a roentgenogram was taken because of a fractured clavicle. This revealed an area of calcification the size of an almond just below the clavicle and close to the mediastinal shadow. The reaction to the Mantoux test was positive; at the age of 17 months this reaction had been negative. Under hygienic care the child progressed satisfactorily; even mild pertussis did not ignite the process. Roentgen examination of the chest showed no marked change until the child was 6 years old, when the area of calcification began to disappear. A year later there was still more reduction in size of the calcified area, and the mother reported that for some time the child had been coughing up small hard masses which had been thought to be portions of teeth. Two of these were recovered and examined. The larger was 3 mm. across and irregular; it contained no tubercle bacilli. The child is now entirely free from symptoms.

DAFFINEE, Boston.

FIRST INFECTION TUBERCULOSIS DURING CHILDHOOD AND ADOLESCENCE. G. VÂJA, Rev. de la tuberc. **5**:854 (July) 1939.

These observations were made in the military schools of Rumania. The students and personnel were examined clinically and roentgenographically, and the students were given an intradermal cutaneous test for tuberculosis. Of special interest was the development during one year of positive cutaneous reactions in 233 out of 737 students who previously had not been sensitive to tuberculin, or an average of 31.6 per cent. Their ages ranged from 12 to 19 years, and the percentage of positive reactions increased with slight irregularity with the age of the students. The cause of this increase in sensitivity to tuberculin among young men living in favorable surroundings is a little difficult to understand. The author believes that the outside contacts of the older boys offers the best explanation. In 11 subjects clinical evidence of infection developed as follows: serofibrinous pleurisy in 3; pulmonary congestion in 3; prolonged fever with perihilar infiltration in 1, and prolonged grippal fever without localization in 4. In 25 boys roentgen examination revealed changes suggestive of tuberculous infection which had not been present one year previously. In the light of these findings the author urges systematic

tuberculin tests four times a year for all students not sensitive to tuberculin. He emphasizes also that during the interval the same test should be made on all nonsensitive subjects who lose weight, show unexplained fatigue or have episodes of fever or other suggestive symptoms. EUGENE H. SMITH, Ogden, Utah.

VALUE OF SEROLOGIC REACTIONS FOR THE DIAGNOSIS OF HEREDITARY SYPHILIS. S. PETRESCO, O. COMAN and E. AMZA, Med. inf., Bucaresti **1**:396 (Nov.-Dec.) 1939.

Comparative examination of the Bordet-Wassermann, Hecht–mother's milk and Meinicke reactions shows that in the presence of hereditary syphilis the last two methods give the largest percentage of positive reactions. The Bordet-Wassermann reaction with cholesterol antigen shows a greater sensitivity than is observed with the Bordet-Ruelens antigen. The reactions were 100 per cent positive in the presence of congenital syphilis. In the presence of latent or inherited syphilis 24 per cent of the reactions were positive. Positive reactions were more frequent with the serums of the mothers than with those of the children. These methods, because of their sensitivity, can prove of great service in the discovery of hereditary syphilis. However, if the results are doubtful or negative, they must always be controlled by the clinical findings, in order to prevent possible failures. Failures may be ascribed in part to nonspecific reactions, or even to too great sensitivity of the mothers.

FROM AUTHORS' SUMMARY.

ALLERGIC PHENOMENA IN CONNECTION WITH TUBERCULOSIS IN CHILDREN. D. MÓRITZ, Orvosi hetil. **83**:827 (Aug. 26) 1939.

Dealing with allergic phenomena in connection with tuberculosis, Móritz describes particularly the so-called "perifocal inflammations" (primary and secondary infiltrations). He regards pleurisy, as well as erythema nodosum and phlyctenular conjunctivitis, as an allergic tuberculous phenomenon.

GÖTTCHE, Budapest, Hungary.

AUTO-INHIBITION IN WASSERMANN'S REACTION. BÖRJE OLHAGEN, Acta med. Scandinav. **102**:654, 1939.

Natural autoinhibition was observed in 30 patients. Two thirds of these suffered with severe disease of the liver and showed a positive reaction to the Takata-Ara test as well as a high sedimentation rate. In these patients the autoinhibition was not manifested until the serum had been heated to 56 C. (e. g., when the complement of the serum was destroyed by ultraviolet radiation). The protein fraction responsible for this autoinhibition was found to be a globulin fraction.

KAJDI, Baltimore.

Diseases of Blood, Heart and Blood Vessels and Spleen

CALCIFICATION OF THE PERICARDIUM: A REPORT OF A CASE IN A BOY AGED TWELVE. WILLIAM G. LEAMAN and JACOB H. VASTINE II, Am. J. Roentgenol. **43**:35 (Jan.) 1940.

A case is presented in detail of a boy, aged 12 years, who showed a combination of calcification and adherent pericardium resulting in Pick's syndrome with pleural effusion, ascites, large liver and edema of the extremities. Operative relief was attempted. Leaman and Vastine emphasize in their discussion the diagnostically suggestive importance of an extra heart sound heard in middiastole in this patient. They present means of differentiating such a sound from other murmurs and third heart sounds.

An excellent discussion of the incidence, etiology, clinical and roentgen diagnosis of calcification of the pericardium is given. The importance of early diagnosis is emphasized, because of the benefit of surgical treatment.

SQUIRE, Chicago.

THE DELAYED APPEARANCE OF HEART DISEASE AFTER RHEUMATIC FEVER. EDWARD F. BLAND and T. DUCKETT JONES, J. A. M. A. **113**:1380 (Oct. 7) 1939.

One thousand children averaging 8 years of age at the onset of rheumatic fever or chorea were studied over a period of ten years or more. Three hundred and fourteen (31 per cent) had no demonstrable cardiac damage after the initial rheumatic infection. In 79 (25 per cent), evidence of valvular heart disease developed in the interval.

Repeated attacks and combinations of symptoms produced more severe heart disease, while uncomplicated chorea and single attacks lessened the incidence and severity of the disease. Eleven of the 79 patients died, 10 as a result of recrudescence of the rheumatic fever. After the ten year period the chance of development of heart disease was slight.

HEERSMA, Kalamazoo, Mich.

CEREBRAL VASCULAR LESIONS ACCOMPANYING SICKLE-CELL ANEMIA. J. M. ARENA, J. Pediat. **14**:745 (June) 1939.

Arena reports on 5 patients with sickle cell anemia, 4 boys and a girl, ranging in age from 4 to 10 years, all of whom suffered from signs and symptoms indicative of cerebral vascular lesions. Autopsy on one of these patients revealed that the large subarachnoid cerebral arteries had undergone gradual obliteration with final closure through a pathologic process identical with that which results in occlusion of the splenic arteries. The cause of the tendency to capillary engorgement and arterial thrombosis is not definitely known. One theory, that the distorted shape of the red blood cells prevents their ready passage through the capillaries, probably explains the general vascular stasis, which is aided perhaps by the tendency of these cells to agglutinate. Other factors, such as fever and infections, probably contribute to the tendency to capillary engorgement and arterial thromboses. Arena suggests that the removal of a large spleen from a child with a history of previous vascular accident and with constitutional symptoms should be given further trial. This suggestion is made because of the similarity between certain constitutional symptoms associated with this disease and those associated with other true hemolytic anemias, such as hemolytic icterus and erythroblastic anemia.

RAUH, Cincinnati.

LYMPHOMAS, LEUCEMIAS AND ALLIED DISORDERS IN CHILDREN. LLOYD F. CRAVER, J. Pediat. **15**:332 (Sept.) 1939.

This article gives a brief survey of 8 cases of Hodgkin's disease, 7 cases of lymphosarcoma, 10 cases of leukemia, 16 cases of enlarged thymus and 1 case of infectious mononucleosis observed in children since 1931. The similarities and differences of these diseases in children and in adults are stressed.

RAUH, Cincinnati.

BLOOD AND LYMPH VESSEL TUMORS IN CHILDREN. WILLIAM L. WATSON, J. Pediat. **15**:401 (Sept.) 1939.

Hemangiomas may be divided into four clinical types. The first group includes the naevus venosus, or port wine stain. In the second group are found cavernous hemangiomas. In the third group the tumors are located more deeply, often covered by normal skin, with a bluish tint imparted to the skin by the underlying tumor. Various combinations of groups 2 and 3 make up the fourth group. The first group of tumors may be treated by repeated blistering doses of ultraviolet ray, solid carbon dioxide applied for ten to fifteen seconds or surgical excision and skin grafting. If extensive, this type of hemangioma is best left untreated. The cavernous hemangiomas are radiosensitive and have been successfully treated by radium or by roentgen rays. Surgical excision of small growths is satisfactory. Watson has successfully treated cavernous hemangiomas around the eye by injec-

tion of 5 per cent sodium morrhuate. Lymphangiomas may be grouped into three definite clinical types: capillary, cavernous and cystic, or cystic hygroma, types. The capillary lymphangioma should be surgically excised. The cavernous type is radiosensitive, and good cosmetic results are obtained by the use of interstitial radium. The cystic lymphangiomas, if removable, should be excised. Withdrawal of fluid and repeated injection of sodium morrhuate gave satisfactory results in 1 case.

RAUH, Cincinnati.

NUTRITIONAL ANEMIA: A FURTHER SURVEY OF DEBILITATED CHILDREN IN MANCHESTER. ANNE SOMERFORD, Brit. J. Child. Dis. **37**:1 (Jan.-March) 1940.

This report is based on a study of 201 children who attended the outpatient department of the Royal Manchester Children's Hospital, in England. Subjects showing organic causes of anemia and debility were eliminated from the study. In every case studied the child was undernourished, and between 50 per cent and 60 per cent of the children had nutritional anemia.

The malnutrition and nutritional anemia were attributed to three main factors: (1) poverty, (2) slackening in home discipline and (3) some psychologic influence.

LANGMANN, New York.

ERYTHROBLASTIC ANAEMIA WITH KYPHOSIS AND CIRRHOSIS OF LIVER. N. D. PATEL and Y. M. BHENDE, Indian J. Pediat. **6**:217 (Oct.) 1939.

A fatal case of moderate anemia with a high erythroblastic reaction, mongolism, osseous changes, increased resistance of red blood cells and osteochondral dystrophy of a dorsal vertebra, associated with kyphosis, cirrhosis of the liver and ascites, occurring in a 5 year old Brahmin boy is described.

GONCE, Madison, Wis.

DRIP TRANSFUSION. A. GRIMBERG, Presse méd. **47**:1399 (Oct. 11) 1939.

Since 1935, drip transfusion (continuous administration of blood in large amounts) has been gaining favor. It is of primary use in operative cases in which the loss of blood is severe or to bring up the hemoglobin level in cases of secondary anemia. Considering that blood represents one eleventh of the body weight and that 500 cc. of blood raises the hemoglobin content 9 or 10 per cent, the amount needed can be calculated. For a baby weighing 7¾ pounds (3,515 Gm.) a transfusion of 45 cc. is approximately equivalent to one of 1 liter for an adult. Heparin, in the opinion of the author, is the ideal anticoagulant for use in this type of transfusion.

DAFFINEE, Boston.

THE DIAGNOSIS OF INFECTIOUS MONONUCLEOSIS BY SEROLOGIC METHODS. R. DEMANCHE, Presse méd. **47**:1614 (Dec. 16) 1939.

Demanche has studied the efficiency of the heterophile antibody test in the diagnosis of infectious mononucleosis. In 57 clinical cases of the disease positive results were obtained, with titration values ranging from 1:56 to 1:57,344. As a control series, 182 observations were made on a variety of conditions, including leukemia, purpura, Hodgkin's disease and various forms of adenopathy. Two false positive reactions were obtained, one in a case of diabetes and another in a case of arthritis.

The reaction does not appear as early as the typical blood picture and reaches its highest point in the second week of the disease. A positive reaction may be present as long as two hundred and forty days.

Demanche concludes that the reaction provides a more precise test than the blood smear. It provides an early diagnosis in ruling out leukemia. It cannot, however, be considered an absolute test until bacteriologic and experimental evidence of the cause of infectious mononucleosis is produced.

DAFFINEE, Boston.

INSULIN ABSORPTION AS A CIRCULATORY TEST IN CHILDREN. H. HUNGERLAND, Ztschr. f. Kinderh. **61**:157 (Aug. 9) 1939.

On the strength of an observation regarding characteristic differences in urinary constituents of normal children and of those with circulatory failure in the sitting position as compared with the recumbent position, the author conducted experiments in which curves indicating the content of sugar in the blood were studied after injection of insulin into the lower extremity. In normal children a similar curve was observed for the prone and for the sitting position. Children with cardiac decompensation or circulatory insufficiency (those with a tendency to orthostatic collapse, vasolability and asthenia) showed the usual decrease in the value of or sugar in the blood when in the recumbent position but practically no change when in the sitting position, demonstrating that considerable stasis occurs in the lower extremities in the sitting position. SIEMSEN, Chicago.

PECULIARITY OF BLOOD FORMATION IN INFANTS AND CHILDREN, PARTICULARLY IN REGARD TO CERTAIN FORMS OF ANEMIA. P. SVASTITS, Orvosképzés **29**:39 (Jan.) 1939.

Since the blood-forming system of newborn and other infants is characterized by great lability, slight excitement can cause great trouble in the formation of blood; on the other hand, the regenerating power is great. Infants can often be observed to have anemia which seems severe and yet can recover quickly. Anemia of prematurity must be attributed to an inability of the hematopoietic tissue to meet the demands of blood formation, which, owing to the rapid growth of the body, are probably great at the time of the premature birth. There is only a quantitative difference between the hypochromic anemia of healthy children and the anemia of prematurity. Nutritional anemias are today much rarer than formerly. During the last seven years Svastits did not find even 1 case of anemia with the Jaksch-Hayem syndrome. GÖTTCHE, Budapest, Hungary.

THE SIGNIFICANCE OF CIRCULATION IN THE PATHOGENESIS OF EXTRARENAL AZOTEMIAS. P. GÖMÖRI, L. PODHRADSZKY and J. KRING, Acta med. Scandinav. **102**:591, 1939.

Extrarenal azotemia is the consequence of deteriorated renal function due to dehydration and salt (sodium) deficiency in cases of vomiting, diarrhea, diabetic coma and adrenal insufficiency. Experimental proof is given that the filtration pressure is diminished and the blood flow reduced in those conditions. While the azotemia following severe hemorrhages can be explained on the basis of hemodynamic changes, in the presence of congestive heart failure, the diminished blood supply to the kidneys is caused by a central factor. The beneficial effect of hypertonic saline solutions is due to restoration of the concentration of sodium as well as to the fact that such solutions open the precapillary arteries, as indicated by measurement of capillary blood flow or by simultaneous measurements of arterial and venous pressure and of cardiac output. The hypochloremic calcium nephrosis has no particular clinical importance. KAJDI, Baltimore.

Diseases of Nose, Throat and Ear

MICROTIA AND CONGENITAL ATRESIA OF THE EXTERNAL AUDITORY CANAL: DEMONSTRATION OF THE EXTERNAL AUDITORY CANAL BY MEANS OF TOMOGRAPHY. J. D. CAMP and E. P. ALLEN, Am. J. Roentgenol. **43**:201 (Feb.) 1940.

A technic is described whereby the external auditory canal is shown in a coronal section and in a sagittal section. Films of the opposite side should be taken for comparison. The majority of cases of microtia are associated with other

lesions, such as atresia of the external canal or defects in the ossicles or labyrinth. This technic should be useful in the investigation of atresia due to trauma or infection and in the demonstration of osteoma of the canal. SQUIRE, Chicago.

MASTOIDITIS IN CONGENITALLY DEFORMED EARS. A. T. WANAMAKER, Ann. Otol., Rhin. & Laryng. **48**:140 (March) 1939.

The author reports 2 cases of mastoiditis in congenitally deformed ears. One patient had a rudimentary ear with complete atresia of the external canal, with the hearing normal on the good side and 65 per cent below normal on the involved side. The second patient had a normal ear on one side, with the other about half the normal size and somewhat deformed, with a small external canal. The hearing was fair, with perception in the Weber test referred to the involved side. Operation on the first patient showed no external canal and no drum. Culture showed streptococci. About thirteen months postoperatively the loss of hearing was 38 per cent by air and only 5 per cent by bone. Operation on the second patient exposed a cholesteatoma, and the culture was negative. There was no drum, and no ossicles were found. The condition in the first case the author felt was caused by infection via the eustachian tube from the throat, and that in the second he concluded was primary cholesteatoma.

It is pointed out that the middle ear and the eustachian tube are developed from the remains of the first brachial cleft, while the pinna and the external meatus are developed from the soft parts overhanging the posterior margin of the same cleft. The external ear may be almost wanting and the external canal completely obliterated, or there may be only a slight defect of the pinna or a membranous obstruction of the canal. Wittmaack stated the belief that the ossicles develop about the fifth month of intrauterine life and, therefore, that what is found in undeveloped ears depends on the month of intrauterine life in which development is arrested. In the absence of a congenital defect in an ear it is hard to believe in primary cholesteatoma, but it is stated that apparently such cases have been reported.

The author urges immediate and thorough examination, with roentgen observation, of any patient complaining of pain in the mastoid region of a congenitally deformed ear. He feels, too, that a discharge from such an ear should give rise to suspicion of involvement of bone and probable primary cholesteatoma.

M. V. MILLER, Philadelphia. [ARCH. OTOLARYNG.]

DIAGNOSIS AND TREATMENT OF DISEASES OF THE EAR IN CHILDREN. HORACE JAMES WILLIAMS, J. A. M. A. **113**:990 (Sept. 9) 1939.

Better care of the ears in infancy and early childhood will lessen deafness in later life. In a large series of cases of aural infections associated with contagious diseases and with other infections, early paracentesis decreased the chance of involvement of the mastoid. The more chronic and late developing types of infections in the ear are often due to chronic sinusitis.

Obstructive lymphoid tissue is a frequent cause of aural infections. When there is any impairment of hearing, early treatment may avert progressive deafness.

HEERSMA, Kalamazoo, Mich.

OBSERVATIONS ON 1,136 CASES OF ENLARGED TONSILS AND ADENOIDS. CHRISTOPHER ROLLESTON, Brit. J. Child. Dis. **36**:251 (Oct.-Dec.) 1939.

This study throws no new light on the subject and suffers because of a lack of follow-up examinations. Only 331 of the children were reexamined. Such statements as "there appears to be a definite relationship between dental caries and the enlargement of tonsils" and "there appears to be a relationship between enlarged tonsils and goitre," need corroboration. LANGMANN, New York.

MALFORMATION OF THE AURICLE. A. LASKIEWICZ, Rev. de laryng. **60**:332 (April) 1939.

Four cases of malformed auricles, classified as follows, are described: (1) crus supratragicum (Gradenigo); (2) aplasia auriculae totalis, with a cleft palate and a branchial cleft opening on the cheek; (3) auriculae accessoriae, with exostoses of the extended canal, and (4) microtia, with hemiatrophy of the skull.

BATSON, Philadelphia. [ARCH. OTOLARYNG.]

SURGICAL MANAGEMENT OF THROMBOSIS OF THE CAVERNOUS SINUS (A NEW OPERATIVE EXPERIENCE). T. GERMAN, Monatschr. f. Ohrenh. **73**:387 (June) 1939.

The author advises that the upper petrosal sinus be followed in approaching the thrombosed cavernous sinus. By using fine gages he was able to reach the region of the cavernous sinus without touching the labyrinth and the internal meatus and to clear out all thrombotic masses. A part of the wall of the superior petrosal sinus was also excised. The patient, a boy of 13 who had had repeated attacks of mastoiditis requiring surgical intervention since infancy, recovered completely.

LEDERER, Chicago. [ARCH. OTOLARYNG.]

OTITIS MEDIA IN TWINS. YUHEI NISHIURA, Oto-rhino-laryng. **45**:718 (July) 1939.

The author reports his observations on 3 pairs of identical twin brothers, aged 3 months, 8 years and 15 years respectively, and 1 of a pair of dissimilar sisters, aged 12 years, in whom acute otitis media developed.

In the 3 pairs of identical twins the onset, the progress, the amount and character of otorrhea and the roentgen observations on the mastoids were identical, though the appearance of the tympanic membranes was different during the course of the disease.

In the dissimilar twin sisters, aged 12 years, both mastoids were underdeveloped. Otitis media occurred in only 1 sister, two weeks after an acute cold. The patient had numerous attacks of otitis media, while her twin sister was perfectly free from aural infection.

The author also conducted a comparative study on the nose, paranasal sinuses, teeth and larynx in the identical twins and found them similar.

HARA, Los Angeles. [ARCH. OTOLARYNG.]

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE CONGENITAL FACTOR IN ACQUIRED DIVERTICULOSIS OF THE JEJUNUM AND ILEUM. G. H. BUNCH, South. M. J. **32**:919 (Sept.) 1939.

The author reports a case of multiple abdominal hernia associated with extensive acquired diverticulosis of the jejunum and ileum.

Each condition was seemingly caused by congenitally defective musculature.

The case is unusual in that multiple gross lesions have resulted from developmental defects in both striated and nonstriated muscle in the same person.

SCHLUTZ, Chicago.

DIVERTICULA OF THE ALIMENTARY TRACT. R. M. HOWARD, South. M. J. **32**:921 (Sept.) 1939.

The author states that the symptoms of diverticula of the gastrointestinal tract, in whatever part they are found, come from the same causes: retention, pressure and inflammation.

Most diverticula of the gastrointestinal tract are symptomless and require no treatment.

Medical management is often advisable and effective in relieving the symptoms. Operation may be necessary if complications are present.

SCHLUTZ, Chicago.

CONGENITAL ABNORMALITIES OF THE GALLBLADDER AND EXTRA-HEPATIC DUCTS. E. STOLKIND, Brit. J. Child. Dis. **36**:115 (April-June); 182 (July-Sept); 295 (Oct.-Dec.) 1939.

This article, in three sections, consists of a review of 245 reported cases with reports of 31 unpublished cases.

The three types of cases of congenital abnormality of the gallbladder that are dealt with are (1) cases of complete absence of the gallbladder; (2) cases in which the gallbladder is represented by a fibrous cord, and (3) cases in which it is found in a rudimentary form.

Congenital abnormalities of the biliary tract may be due to faulty development or to inflammation, to the latter probably when the gallbladder is represented by a fibrous cord and to the former when there is complete absence of the gallbladder and the extrahepatic ducts. There may also be cases in which both causes operate.

On a number of the infants in the series of 31 unreported cases exploratory laparotomy was performed in the hope of correcting the abnormality, but all died within twenty days of the operation.

In many of the cases additional congenital malformations were present.

LANGMANN, New York.

VON GIERKE'S DISEASE. F. R. B. ATKINSON, Brit. J. Child. Dis. **36**:261 (Oct.-Dec.) 1939.

Atkinson reviews the 2 cases of the disease (hepatonephromegalia glycogenica) described by von Gierke in 1929 and numerous other examples recorded in the literature, which now includes 59 certain cases.

The age incidence, symptoms, signs, biochemical data and necropsy observations are taken up in some detail.

LANGMANN, New York.

ABDOMINAL PAIN IN YOUNG CHILDREN. V. SMALLPEICE, Practitioner **143**:199 (Aug.) 1939.

The author discusses briefly a large number of causes of abdominal pain. Acute appendicitis stands out as the most important both from its frequency and from the necessity for immediate action. As to the other emergencies, the general character of acute intestinal obstruction must be appreciated; once obstruction has been diagnosed, treatment passes to the surgeon, and although an accurate picture of the cause is of academic interest to the general practitioner, it is not of such vital importance as is fundamental recognition of the intestinal obstruction itself.

Because the margin of safety between appearance of symptoms and the need for action may be so small, there is no complaint in early childhood with which time is more important. To give a few comforting words over the telephone and postpone a visit until morning is to risk a fatal result. The parents' responsibility is also considerable; they may fail to report the earliest symptoms, or, worse, may administer a purgative which will do untold harm; they may present the unfortunate practitioner with a screaming, uncontrolled child who obstructs all efforts at examination and with whom palpation of the abdomen is almost impossible. Prognosis is "loaded" from the start against such a child. If a friendly relation can be established between the physician and his small patient during health it is of the greatest value in time of illness, and this constitutes yet another strong argument in favor of routine medical examination of the healthy child.

GELSTON, San Francisco.

DICTYOCYTIC RETICULOSARCOMA. D. G. EDWARD, Proc. Roy. Soc. Med. **32**:1171 (July) 1939.

The case of a boy aged 5½ years is reported. He was admitted to the hospital on account of pyrexia, swelling of the abdomen, loss of weight and headache following pertussis five months previously. The liver was found to be enlarged, and a hard mass of lymph glands in the left iliac fossa and on the left lateral wall of the pelvis (felt per rectum) was observed. A diagnosis of Hodgkin's disease was made, but a biopsy was not done on account of the absence of a superficial lymph gland. The investigations made at this time are given in the report. The patient was discharged but was readmitted three months later with the same physical signs except that there were a few enlarged glands in the right groin. A biopsy was made on a section of one of these nodes, and the pathologist reported that the histologic appearances were those of a dictyocytic recticulosarcoma. The boy was given blood transfusions and high voltage roentgen therapy. The treatment caused some shrinkage of the iliac glands; the patient appeared brighter, and his temperature remained lower. WILLIAMSON, New Orleans.

ETIOLOGY AND PATHOLOGY OF THE TOXICOSES OF INFANCY. K. JONSCHER, Presse méd. **47**:583 (April 19) 1939.

Jonscher considers the true cause of the toxicoses encountered in early infancy to lie between the commonly accepted hypotheses. Toxicosis in all cases has a background in an underlying constitutional defect interfering with digestion. The ensuing disturbance varies according to which of the great functions of the body (metabolism or immunity) is involved. Jonscher divides his cases into two groups, cases of alimentary toxicosis (primary disturbances of metabolism) and cases of infectious toxicoses (disturbances involving loss of immunity). The two forms differ in some minor details, but the chief differences are summed up thus:

Alimentary Toxicoses	*Infectious Toxicoses*
1. Drowsiness is marked.	1. Drowsiness is less marked; the infant is sick, not apathetic.
2. Dehydration is present; cutaneous elasticity is lost.	2. Dehydration is less apparent, especially in older infants.
3. There is concentration of the blood volume (serum protein increased).	3. The serum protein is increased only slightly and does not fall as rapidly when treatment succeeds.
4. The roentgen shadow of the heart is smaller than normal, and the diaphragm is low.	4. No changes are revealed in roentgenograms of the chest.
5. Albuminuria is always present.	5. Albuminuria is rare.

DAFFINEE, Boston.

ACUTE PERITONITIS IN CHILDHOOD. J. DUZÁR, Orvosképzés **29**:722 (Sept.) 1939.

Duzár deals with the diagnostic difficulties which occur when the suspicion of acute peritonitis arises. These difficulties are especially great in the case of children, for many children localize their most varied pains in the abdominal region.

GÖTTCHE, Budapest, Hungary.

OPERATIVE TREATMENT OF CONGENITAL CEREBRAL HERNIA. N. I. SOKOLOV, Vestnik khir. **57**:593 (June) 1939.

Sokolov has reviewed all cases of congenital encephalocele reported by Russian surgeons. Of the 143 patients, 119 underwent an operation; of these, 43 died, the mortality rate being 36.1 per cent. Of the 107 patients with frontal ethmoid

encephalocele, 36 (33.6 per cent) died; in 3 (2.8 per cent) the results seem doubtful. Recovery was obtained in 68 (63.6 per cent). The author reports 8 cases observed by himself and offers his own plastic technic for hernia. His conclusions are as follows: 1. Frontal ethmoid encephalocele is more common in the Soviet Republic, the occipital variety being rare. 2. Infants with frontal ethmoid cerebral hernia display remarkable viability. 3. Infants with cystic encephalocele should be operated on at the earliest possible time, even during the first days of life. In cases in which the condition is doubtful treatment may be postponed till the infant is a month old, but it should always be performed in the first year of life. 4. In cases of considerable bony defect the symptoms may seem grave, but they disappear after the plastic closure of the defect. 5. The inner opening of the bony canal in cases of nasofrontal hernia has unequal axes, the transverse axis usually exceeding the others; this is especially true in nasoethmoid hernia. The shape of the inner opening of the bony canal approaches an oval, the edges being fairly even. 6. The author recommends a one stage, external operation, the procedure for posterior orbital hernia being an exception to the rule. 7. In cases of nasoethmoid and nasofrontal encephalocele the closure of the inner opening of the canal with a bony graft inserted from the inside of the skull insures good results. The access to the inner opening is gained by means of mobilizing the anterosuperior and partly the lateral walls of the bony canal. A graft larger than the defect and completely covering it can be introduced into the cranial cavity without difficulty, for which purpose the difference in the axes of the canal is utilized. 8. In cases of anterior orbital hernia the short narrow canal should be completely eliminated by the introduction of a pinlike cartilaginous graft. 9. The author believes a free bony autoplastic graft to be the best material for the closure of large defects in cases of encephalocele, the cartilaginous autoplastic graft being the best for smaller defects.

J. A. M. A.

Nervous Diseases

ELECTROENCEPHALOGRAPHY IN EPILEPSY. F. A. GIBBS, J. Pediat. **15**:749 (Dec.) 1939.

Gibbs discusses the types of encephalographic tracings found in petit mal, grand mal and psychomotor attacks. Illustrations of normal tracings and of those of patients with epilepsy are included in the report. The great similarity between the activity of the cortex and the activity of the respiratory center is stressed. Brain waves are about sixty times faster than respiratory waves. A great variety of factors which alter the frequency of respiration alter the cortical frequency in the same direction; e. g., sleep, sedatives and low carbon dioxide inhalation slow both cortical and respiratory rhythms, and fright, sensory stimulation and high carbon dioxide inhalation speed up both cortical and respiratory rhythms. Increase in carbon dioxide inhalation is effective in preventing or stopping the Cheyne-Stokes-like rhythm of petit mal, and low carbon dioxide inhalation readily precipitates petit mal seizures. Sedative drugs are particularly effective against the hyperpnea-like activity of the cortex in grand mal but are relatively ineffective and may be harmful when used against the Cheyne-Stokes-like rhythm of petit mal and the abnormally slow rhythm of psychomotor attacks. Patients with petit mal tend to have a lower carbon dioxide content of the blood than normal persons and patients with grand mal tend to have a higher carbon dioxide content. Patients with petit mal show high carbon dioxide content of the arterial blood on days when few seizures occur and a low carbon dioxide arterial content on days when many seizures occur. Day by day examination of the arterial blood of patients with grand mal reveals an increase in carbon dioxide until a seizure occurs, and after the seizure a fall in carbon dioxide. Electroencephalography has illustrated the severest paroxysms of cerebral dysrhythmias and the continuous disturbances of the cerebral beat which occur between the

paroxysms, and has disclosed many persons with disorders of the cortical beat who show no symptoms generally recognized as epilepsy. Among these are many problem children, persons with disorders of personality and approximately one-half the near relatives of persons with epilepsy.

RAUH, Cincinnati.

PLACE OF ENCEPHALOGRAPHY IN PROGNOSIS IN CHILDHOOD. J. K. BRINES and E. LORD, J. Pediat. **15**:836 (Dec.) 1939.

Six case reports are presented to illustrate the serious error which may be made when an unfavorable prognosis as to the mental adequacy of a child under 3 is given on the basis of the encephalographic findings. The authors suggest that the encephalographic standards for infants are relatively unreliable and that more knowledge is needed as to the resumption of growth and development after disease or cerebral injury.

RAUH, Cincinnati.

ACUTE LYMPHOCYTIC CHORIOMENINGITIS. C. J. TRIPOLI and D. E. FADER, New Orleans M. & S. J. **92**:308 (Dec.) 1939.

First described as a clinical entity by Wallgren under the name "acute aseptic meningitis," this disease is now known chiefly as acute lymphocytic choriomeningitis. The causative agent seems to have been established as a virus and has been isolated by various workers in several epidemics. The disease is readily transmitted to monkeys, guinea pigs, white mice and white rats. The incubation period in monkeys is six to eight days; the time for the human subject is not known.

The clinical picture is characteristic. After a few days of mild prodromal symptoms, there is a sudden onset. The outstanding symptoms, in the order of their appearance, are fever, headache, drowsiness, rigidity of the neck, nausea and vomiting. The range of temperature is from 100 to 103 F. If the illness is severe, there may also be backache, abdominal pain, mental confusion and marked drowsiness, with occasional convulsions, opisthotonos and loss of consciousness. The Kernig sign is usually positive.

The spinal cell count runs from 250 to 500 cells per cubic millimeter, with extremes of 50 to 3,000. Lymphocytes usually predominate, though polymorphonuclear cells may be found running as high as from 10 to 30 per cent. The sugar and chloride contents of the fluid are normal; the protein is low—plus 1 to plus 2. The white blood cell count ranges from 2,000 to 12,000, with 60 to 75 per cent polymorphonuclear cells.

Symptoms are rapidly alleviated after a single lumbar puncture, often so abruptly as to suggest the crisis in lobar pneumonia. The usual duration of the illness is from five to sixteen days, with an average of six to ten days. In the 12 cases reported there were no fatalities and no sequelae; in these respects this series corresponds with previously reported series.

A provisional diagnosis may be made if the following criteria are met: (1) an acute onset of meningeal symptoms; (2) changes in the cerebrospinal fluid characteristic of meningeal irritation, with a slight or moderate increase in the number of cells, especially in that of lymphocytes; (3) sterility of the fluid both on direct examination and in appropriate culture mediums; (4) a short duration of mild illness, without complications; (5) the absence of any condition which might lead to meningeal irritation, such as otitis media or acute or chronic infection, and (6) the absence in the community of any disease which characteristically involves the central nervous system.

The diseases which may present a similar picture are tuberculous meningitis, abortive poliomyelitis, meningovascular syphilis and lead encephalitis.

The treatment recommended is lumbar puncture and if the condition is severe, administration of human convalescent serum.

Twelve cases are reported, all furnishing the factual data required for diagnosis. The patients ranged in age from 1 to 23 years. There were 8 males and 4 females.

BERKLEY, Los Angeles.

ENCEPHALOGRAPHY IN INFANTILE NEUROPSYCHIATRIC PRACTICE. R. RUGGERI, Arch. ital. di pediat. **6**:531 (Nov.) 1938.

Ruggeri reviews the literature on the subject, considering the manifold uses of encephalography, and indicates that the use of it in the study of epilepsy is most important. He describes the technic to be followed, the benefits of the procedure and the damages which may be produced.

He studies the normal encephalogram carefully and then reports cases observed in his own clinics, giving encephalograms of 35 children affected with various neuropsychiatric diseases.

He compares his conclusions with those of others and demonstrates that encephalograms show that hydrocephalus is the cause of a considerable number of disturbances of the visual apparatus. Encephalograms may also show very early whether hydrocephalus is developing in consequence of meningitis.

The encephalographic examination, the author states, should never be omitted in the investigation of any grave nervous disease and particularly in that of epilepsy, in which sometimes the cause of the illness may be demonstrated by it.

The monograph is comprehensive and should be read to appreciate its value. A detailed bibliography follows.

PREVITALI, New York.

CAUSES AND GENESIS OF EPILEPSY. L. BARRAQUER, Med. inf., Rome **10**:293 (Oct.) 1939.

Statistics on 260 epileptic persons in Barcelona, Spain, indicate that 49 per cent had a neuropathic heredity and 36 per cent a history of obstetric trauma or severe toxic infection in infancy. Postmortem studies confirm the opinion that in hereditary epilepsy there is true cellular abnormality of the brain.

HIGGINS, Boston.

SEVERE EPILEPTIC SYNDROME IN A CHILD WITH PARIETAL ENCEPHALOCELE. F. FONTANA, Pediatria **47**:517 (June) 1939.

A 6 year old girl had an encephalocele in the right parieto-occipital region. For a period of four years she had had convulsions after high fever. These convulsions then became spontaneous, more frequent and of longer duration. Operation disclosed an adhesion between the scalp and the dura and an adhesion between the dura and the brain. The breaking up of these adhesions brought about relief from the nervous symptoms.

MARTOCCIO, Utica, N. Y.

LATENT PERIODS IN THE DEVELOPMENT OF BRAIN TUMORS. NEWENA KOJEWA, Monatschr. f. Kinderh. **79**:256 (Aug.) 1939.

The tumors described occurred in 3 children, aged 14 months, 15 months and 4 years. Two specimens are photographed. The unusual feature common to these children was a prolonged period without diagnostic symptoms. The condition in the first patient was characterized for many months by severe vomiting and anorexia. In the second a syndrome developed resembling Simmonds' disease. In the third there were no symptoms until there was a sudden hemorrhage into the tumor.

GERSTLEY, Chicago.

EXPERIMENTAL STUDY ON THE VITAMIN B_1 CONTENT OF THE CEREBRAL SPINAL FLUID OF THE INFANT AND SMALL CHILD. M. GEORGESCU and D. TIMUS, Med. inf., Bucaresti **1**:317 (July-Aug.) 1939.

Georgescu and Timus experimented on pigeons presenting the typical phenomena of beriberi, injecting cerebrospinal fluid taken from normal children and from children showing meningitis. The fluid was taken both before and after intravenous injections of vitamin B_1. Judging from the therapeutic effects on the pigeons, the authors estimated the presence and the passage of vitamin B_1 into the cerebrospinal fluid and arrived at the following conclusions: 1. The cerebro-

spinal fluid of the normal infant under 2 years of age contains only minimum quantities of vitamin B_1. 2. Vitamin B_1 when injected intravenously does not pass into the cerebrospinal fluid if the meninges are normal. 3. Previous to the injection of vitamin B_1 the cerebrospinal fluid from children with meningitis shows only a minimum quantity of vitamin B_1. 4. After introduction of this vitamin into the blood in cases of meningitis the cerebrospinal fluid becomes rich in vitamin content, thus acquiring the property of curing experimental beriberi.

LESLIE, Evanston, Ill.

GENESIS OF EARLY ACQUIRED HYDROCEPHALUS. O. ELO and E. OTILA, Acta pædiat. **23**:503, 1939.

Elo and Otila submit a textbook synopsis of the pathologic aspects and the genesis of hydrocephalus, laying special emphasis on the point that injurious influences exert a much more destructive effect when they are brought to bear on the immature brain than when they operate on the central nervous system of the older subject. Two illustrative cases are described. In the first, intrauterine obliteration of the aqueduct as the result of a disturbance of development led to almost complete destruction of the brain and supplied the substrate for the development of hemorrhagic encephalitis. The second case resembled the first but was complicated by the presence of pyogenic meningitis of postnatal origin. This is a long paper. The protocols are unusually complete, and the bibliography is serviceable.

McCUNE, New York.

Psychology and Psychiatry

DETERMINING AND NUMERATING ADJECTIVES IN CHILDREN'S SPEECH. JOHN B. CARROLL, Child Development **10**:215 (Dec.) 1939.

Limiting adjectives may be classified as (1) determiners, e. g., "the," "this," "that;" "a," "any," "each," "some," and (2) numeratives, e. g., "all," "both," "few." Many of these words may also be used as pronouns. Analysis of samples of the speech of 887 children aged 2½ to 4½ years showed significant age trends in the frequency of determiners and numeratives and corresponding pronouns, but the proportion of these words to the total number of words remains fairly constant. The article "a" ("an") appears earlier than "the." Relative to the adjectival use, the pronominal use of determiners and numeratives decreases from 2½ to 4½ years of age. An attempt is made to outline the processes involved in the learning of the determiners and numeratives, the principle of differentiation from "phrase-wholes" being used.

CARROLL, Minneapolis.

THE MEASUREMENT OF ATTITUDES OF DELINQUENT AND NORMAL BOYS BY USE OF AN ASSOCIATIONAL TECHNIQUE. WILLIAM FAUQUIER, Child Development **10**:231 (Dec.) 1939.

To investigate Sherman's assumption that "the more insecure an individual feels, the more emotionally toned and stronger are his attitudes," a free association test was given to 40 normal boys who were well adjusted to their home and school environments and to 86 delinquent boys in institutions. On the basis of objectively measured behavior differences the delinquent boys were subdivided into two groups: (1) the institutionally adjusted and (2) the institutionally maladjusted. A quantitative treatment of qualitative differences in response indicated dissimilarities in attitude among the three groups, of which the most striking example was the institutionally maladjusted boys' stronger drive for security and prestige, their greater resentment toward and distrust of other persons and their inferior ability to inhibit violent forms of reaction. The general findings suggest basic differences between the attitudes of delinquent and nondelinquent persons. There is further indicated a marked dissimilarity between the two types of boys in institutions.

FAUQUIER, Canaan, N. Y.

THE ROLE OF THE PEDIATRICIAN IN MENTAL HYGIENE. PAUL H. JORDAN, J. Pediat. **15**:121 (July) 1939.

Jordan discusses briefly some of the more fundamental psychiatric concepts the understanding of which is important to the pediatrician and suggests the manner in which they may be utilized pediatrically.

The first part of this paper outlines and discusses the basic needs necessary to the well-being of every child. These are the need for security, the need for affection and understanding and the need for achievement and recognition. Stresses or inherent weaknesses may frustrate the child in his attempts to obtain satisfaction of certain or all of these basic needs. Inherent weakness may come from within the child or through heredity. Such handicaps as low intellectual endowment and inherent instability of the autonomic nervous system constitute hereditary weakness. Injury at birth, congenital syphilis, rheumatic heart disease and other conditions may be grouped under weakness occurring from within the child. Other important sources of frustration may arise within the home or may come from the environment outside the home.

The second part of the paper outlines the symptoms of the child's mental illness and discusses what maladjustment means as far as the child is concerned. These symptoms are merely a perverted expression of the unhappiness which the child consciously or unconsciously feels. The reaction of the child to his unhappy state is not conscious, for he usually is totally unaware of the factors which cause his condition.

RAUH, Cincinnati.

A PRELIMINARY SURVEY ON THE RELATION OF PHYSICAL DEFECTS TO SCHOLASTIC STANDING. A. C. WOOFTER, West Virginia M. J. **35**:413 (Sept.) 1939.

A study of 360 unselected students was made to ascertain the relation, if any, between physical defects and scholastic class standing and to determine which defects are most detrimental to scholastic progress and should therefore be first chosen for corrective treatment.

It was indicated that infected tonsils caused most days of absence from school and proportionately the greatest lowering of scholastic standing.

Enlarged tonsils stood second to infected tonsils.

Defective vision came next to tonsils in producing a lowering of class standing, and malnutrition followed defective vision.

Because of the small number of cases observed, deafness could not be studied definitely.

SHAWKEY, Charleston, W. Va.

Diseases of the Genitourinary Tract

TREATMENT OF WILMS' TUMOR. IRA I. KAPLAN and MEREDITH F. CAMPBELL, Arch. Pediat. **56**:766 (Dec.) 1939.

The case reported is that of a Jewish boy in whose case the diagnosis of Wilms's tumor was made at the age of 11 months. After surgical intervention and irradiation the child was observed over a period of three and one-half years and was free of recognizable signs of recurrence or metastasis. ORR, Buffalo.

ACUTE NEPHRITIS SIMULTANEOUSLY AFFECTING THREE SIBLINGS. SAMUEL L. ELLENBERG and ALEXANDER T. MARTIN, Arch. Pediat. **57**:38 (Jan.) 1940.

Three cases of acute nephritis appearing simultaneously in a sister and 2 brothers are reported. The question is raised as to the possibility that a greater familial incidence of acute nephritis may be present than has hitherto been reported.

Cases of unsuspected acute nephritis may be discovered if routine urinalysis is performed in the cases of all children recovering from acute infections of the respiratory tract.

ORR, Buffalo.

CANCERS OF THE GENITOURINARY ORGANS IN CHILDREN. ARCHIE L. DEAN, J. Pediat. **15**:340 (Sept.) 1939.

Cancer of the genitourinary tract other than cancer of the kidney is a very rare occurrence in children. Cancer of the penis does not occur in childhood, but circumcision a few days after birth provides the best protection against precancerous changes of the penis which may occur in boys before the age of 10 years. In cases of cancer of the testis the appearance of the tumor is usually the first and only sign. Metastases occur early; therefore every testicular enlargement and intrascrotal swelling should be considered malignant until proved otherwise. Primary testicular tumors should be irradiated and then removed if no metastases are found. If metastasis has occurred, irradiation is the only treatment. The prognosis of cancer of the bladder and prostate is poor, because the tumor is usually not discovered until the late symptoms of obstruction and infection develop. Wilms tumors are the malignant tumors most frequently found in the genitourinary tract in children. The onset is insidious, and a palpable tumor is the most frequent early diagnostic sign. Dean advocates irradiation alone as the most effective treatment for Wilms tumors.

RAUH, Cincinnati.

GYNECOLOGIC CANCER IN CHILDREN. JOHN A. KELLY, J. Pediat. **15**:354 (Sept.) 1939.

Cancer of the genitalia in girls is a rare and usually a rapidly fatal disease. Its presence is to be suspected when vaginal discharge or unusual vaginal bleeding exists. Ovarian tumors are the most frequent forms of cancer of the genitalia in girls. In the author's series of 7 cases of tumor of the female genitalia, 5 of the tumors were ovarian. The average age of the patients was 13½ years; the oldest child was 15 and the youngest 12 years old. Two of these tumors were classed as embryonal carcinomas, 2 as malignant teratomas and 1 as a myxoxanthosarcoma. For operable ovarian tumors surgical removal is indicated. For highly malignant tumors operative intervention should promptly be supplemented by thorough radiation therapy. Of the 5 girls with ovarian tumor, 3 died from recurrent growths or from general metastases; 1 was lost to follow-up, and 1 has been well and free from symptoms for about two years.

RAUH, Cincinnati.

WILMS' TUMOR: REPORT OF A CASE. JOHN H. SHELDON and JOHN W. CANADY, New York State J. Med. **39**:1857 (Oct. 1) 1939.

A report is given of a case of Wilms's tumor in a boy 10 months of age. The kidney and tumor mass weighed 977 Gm. Two months after the operation the other kidney was involved and the child died.

AIKMAN, Rochester, N. Y.

THE VALUE AND USE OF URINARY ANTISEPTICS. FREDERICK J. PARMENTER, New York State J. Med. **39**:1871 (Oct. 1) 1939.

Free drainage is more important than antiseptics. Complete urinary examination is again urged. Urinary antiseptics can be effective only when the kidney has good function.

AIKMAN, Rochester, N. Y.

CONGENITAL ABSENCE OF THE VAGINA. NATHAN P. SEARS, New York State J. Med. **39**:2019 (Nov. 1) 1939.

Sears, in reporting 3 cases of congenital absence of the vagina in which correction was achieved by operation, advises that the operation should be performed only on adults who are definitely female and anticipate marriage. Good results were obtained in the 3 cases. The operation is described.

AIKMAN, Rochester, N. Y.

PYELITIS, MEDICAL ASPECTS. KEMPSON MADDOX, M. J. Australia **2**:927 (Dec. 23) 1939.

The following five forms of pyelitis are recognized:

1. Acute medical, or primary, pyelitis, which is most commonly seen in adolescent girls and young women after exposure to cold or after an infection of the upper respiratory tract. Diagnosis requires careful taking of the history, careful physical examination and microscopic instead of gross examination of the urine. Alkalis are said to be specific for treatment, but sulfanilamide is mentioned as possibly supplanting it eventually.

2. Pyelitis accompanying advanced renal involvement. This is usually part of a more generalized infection of the urinary tract but may require surgical treatment.

3. Asymptomatic urinary infection. This form is usually discovered accidentally, but careful history usually reveals occasional episodes of fever, probably due to acute pyelitis.

4. Imitation of urinary infection. In cases of this condition there are symptoms of anomalies in the urinary tract, such as frequency of urination, but no abnormalities can be discovered.

5. Exogenous urinary infection. This form follows catheterization.

The comparative value of mandelic acid and of sulfanilamide is discussed. Pyelitis of infancy, other than that occurring as a complication of one of the acute fevers, is said to be secondary to some obstruction in the urinary tract. Treatment demands careful examination of the obstruction and the use of mandelic acid or sulfanilamide.

TENNEY, Madison, Wis.

CIRCUMCISION IS AN UNNECESSARY OPERATION. LAVERGNE, Nourrisson **27**:280 (Sept.) 1939.

The author discusses the pros and cons of the problem and is definitely opposed to routine circumcision. All possible complications can be avoided, because the operation never is necessary if, within the first three months of the infant's life, the mother is taught how to retract the prepuce and how to keep it clean. Even if phimosis and inflammation have developed, they can always be treated successfully in a conservative way. Softening of the adhesions with petrolatum and oil, retraction of the prepuce and breaking down of the adhesions with a probe will always be effective if softening has been done sufficiently, with enough patience.

HEYMANN, Cleveland.

HYDRONEPHROSIS SIMULATING DIABETES INSIPIDUS. L. KÜHNER, Kinderärztl. Praxis **10**:486 (Nov.) 1939.

This is a brief description of the observations in the case of a child 3 years of age who was admitted to the University of Heidelberg Children's Hospital with a diagnosis of diabetes insipidus. There were excessive thirst and polyuria; the urine had a low specific gravity, and the general condition of the child was good. Dilution and concentration tests of the urine, however, pointed toward impaired function of the kidneys. Pyelograms revealed the presence of bilateral hydronephrosis.

HEYMANN, Cleveland.

ALKAPTONURIA. D. MÓRITZ, Orvosi hetil. **83**:881 (Sept. 9) 1939.

A 3 year old boy had constant alkaptonuria almost from birth. His father, who is healthy, married twice and has 2 healthy children by the first wife. The patient originates from the second marriage and has a 4 month old brother, who also has alkaptonuria. The mother of these children is healthy, but 1 child of her brother has alkaptonuria. It is obvious that the disease was brought into the family by the second wife.

GÖTTCHE, Budapest, Hungary.

Diseases of the Ductless Glands; Endocrinology

THREE CASES OF MASKED HYPOTHYROIDISM HAVING ABDOMINAL SYMPTOMS. ANTHONY BASSLER, Endocrinology **26**:218 (Feb.) 1940.

It seems that occasionally patients with masked hypothyroidism present themselves with complaints of abdominal pain. They have low blood pressure, leukopenia and a low basal metabolic rate, all of which can be determined by laboratory methods. They are dramatically benefited by thyroid therapy. Why there are abdominal pain and tenderness in this condition is not understood. These symptoms may be neurogenic; they certainly are not due to colonic stasis or to constipation.

JACOBSEN, Buffalo.

THE INHIBITION OF LACTATION POST-PARTUM WITH TESTOSTERONE PROPIONATE. JACOB S. BEILLY and SAMUEL SOLOMON, Endocrinology **26**:236 (Feb.) 1940.

A series of 108 cases of inhibition of lactation post partum by means of testosterone propionate is presented. Complete inhibition occurred in 58 per cent and incomplete results in 40 per cent of the cases. In all these the patient obtained relief from engorgement or distention and from pain or discomfort in the breasts. Failure occurred in 2 per cent of cases.

JACOBSEN, Buffalo.

THE SOJOURN OF INSULIN IN THE BLOOD OF RABBITS AFTER THE ADMINISTRATION OF MASSIVE DOSES OF INSULIN. LEONARD F. JOURDONAIS and MAURICE BRUGER, Endocrinology **26**:250 (Feb.) 1940.

Insulin injected intravenously in massive doses (1,000 units) into rabbits was recovered from the blood stream for sixty to ninety minutes after the injection. After this time insulin was not recovered from the blood by the procedure used, although the effect of insulin as demonstrated by hypoglycemia persisted for as long as nine hours. The largest amounts of insulin recovered were obtained within the first fifteen minutes after injection. Blood extracts prepared later than seventy-five minutes after the injection of massive doses of insulin frequently gave a hyperglycemic response.

Evidence is presented to indicate that massive doses of insulin may so disturb carbohydrate metabolism as to result in ketosis.

JACOBSEN, Buffalo.

THE EFFECTS OF TESTOSTERONE PROPIONATE ON EPIPHYSEAL CLOSURE, SODIUM AND CHLORIDE BALANCE AND ON SPERM COUNTS. E. PERRY MCCULLAGH and F. J. MCGURL, Endocrinology **26**:377 (March) 1940.

Three cases are cited in which large doses of testosterone propionate caused epiphysial union to take place at a more rapid rate than normal. It is stated that this should serve as a warning to those inclined to use large doses of this material for immature persons and that it suggests strongly that dwarfing might be caused by such doses given to patients who have not attained normal adult stature. A temporary fall in total sperm production occurred during the period of therapy.

JACOBSEN, Buffalo.

THE RECOVERY OF TESTES AFTER ANDROGEN INDUCED INHIBITION. R. R. GREENE and M. W. BURRILL, Endocrinology **26**:516 (March) 1940.

The administration of several types of androgenic extracts has been shown by various workers to produce injury and retardation to the testes of normal boys, but the duration of this effect has not been noted. The experiments described were designed to determine the duration of the injurious effects.

Greene and Burrill summarize their results as follows:

"In agreement with previous workers the administration of low doses of testosterone propionate, 0.1 mg. daily for 20 days, caused inhibition of testicular growth in young rats. Seven to 10 months after treatment the testes were normal and no difference was found between treated and control animals with respect to testicular weight, sperm motility, fertility, seminal vesicle and prostate size."

JACOBSEN, Buffalo.

THE EFFECT OF ANTERIOR PITUITARY-LIKE SEX HORMONE ON THE BLOOD PICTURE IN MAN. WILLIAM M. MOFFAT, Endocrinology **26**:595 (April) 1940.

The essential change in both sexes was leukocytosis, which appeared four hours after injection, reached its greatest height at six or eight hours and then diminished but did not disappear at twenty-four hours.

JACOBSEN, Buffalo.

REPEATED GLUCOSE TOLERANCE TESTS IN CHILDREN. HENRY J. JOHN, J. Pediat. **14**:737 (June) 1939.

Repeated dextrose tolerance tests, done on a group of children in the first and the second decade, were studied. The dextrose load was 75 Gm. up to 16 years of age and 100 Gm. after that. Ninety per cent of the curves which were normal at the first test remained normal, and 1 curve, or 10 per cent, later showed diabetes. Of the curves which were diabetic at the first test, 55.5 per cent continued the same and 4 curves, or 45.5 per cent, later became normal. John compares these observations with those obtained for adults; the results suggest that among children the curve is more labile than among adults and that either there are more factors, or else the factors which tend to disrupt temporarily the carbohydrate metabolism are more powerful or more easily overbalanced among children than they are among older persons. Two lists of factors which tend to disrupt the carbohydrate metabolism are included in this report. John discusses the endocrine influence on the carbohydrate metabolism. To the question whether a normal curve indicates that the patient's insulogenic reserve is such that he is absolutely protected from diabetes, the author answers "no." Although a normal curve rarely turns diabetic, such an instance is cited. John concludes that the result of the dextrose tolerance test is fairly stable if care is taken and the test done under standard conditions. There can be a change in the curve in later years, just as there are changes in the function of other organs than the pancreas.

RAUH, Cincinnati.

PRESENT STATUS OF THE ENDOCRINE DISEASES OF CHILDHOOD. F. B. TALBOT, South. M. J. **33**:63 (Jan.) 1940.

The author states that little is known about endocrine glands, despite the great advances of the past few years. If the powerful therapeutic agents are to be employed intelligently and safely, it is necessary to use all available aid in making a diagnosis, so that the proper gland will be treated.

F. W. SCHLUTZ, Chicago.

GENERALIZED MUSCULAR HYPERTROPHY IN INFANCY WITH CONGENITAL HYPOTHYROIDISM (DEBRÉ-SEMELAIGNE SYNDROME). H. DARRÉ, P. MOLLARET, ZAGDOUN and OEHMICHEN, Rev. neurol. **72**:249 (Sept.) 1939.

A case is presented which seems to be typical of this syndrome (generalized muscular hypertrophy, muscular rigidity and hypothyroidism). The infant gained poorly because of inability to nurse properly and because of regurgitation. Muscular hypertrophy was pronounced and involved practically the entire body. The facies, the tongue, the navel, and the skeletal development were indicative of cretinism. Neurologic examination showed no abnormalities. Psychic development was

retarded. The cholesterol content of the blood was 195 mg. per hundred cubic centimeters, with total lipids 616 mg. per hundred cubic centimeters. Thyroid therapy seemed to help the muscular condition as well as the cretinism. The authors present a long argument supporting their diagnosis, with a critical review of similar cases reported in the literature.

DAFFINEE, Boston.

Diseases of the Muscles, Bones, Joints and Lymph Glands

CONGENITAL SYNOSTOSIS OF THE CERVICOTHORACIC VERTEBRAE (THE KLIPPEL-FEIL SYNDROME). A. M. RECHTMAN and M. THOMAS HORWITZ, Am. J. Roentgenol. **43**:66 (Jan.) 1940.

The syndrome is probably due to the irregular segmentation of the spine occurring in the early weeks of fetal life as a result of morbid conditions in the mother interfering with the normal fetal development. The primary clinical characteristics are: (1) shortness of the neck; (2) low implantation of the hair line, and (3) painless limitation of movements of the head and neck on a purely mechanical basis. Secondary clinical characteristics are: (1) scoliosis or kyphoscoliosis; (2) elevated scapulas (Sprengel's deformity); (3) descent of the nipples; (4) torticollis of muscular or osseous origin; (5) disproportion in length between the extremities and of the trunk, and (6) defects in other parts of the body, often congenital. Pathologically, some or all of the following are seen: reduction in the number of cervical vertebrae with fusion, superior cervical spina bifida, elevation of the thoracic cage, platyspondylisis, cervical and fused ribs and other congenital abnormalities. These are easily seen roentgenographically by use of the positions outlined by the authors.

The authors present reports of 3 typical cases of Klippel-Feil syndrome and 2 cases of congenital synostosis of the cervical vertebrae, the latter representing intermediary phases of cervical maldevelopment.

SQUIRE, Chicago.

OSTEOPETROSIS ASSOCIATED WITH HODGKIN'S DISEASE: REVIEW OF THE LITERATURE AND REPORT OF CASE. HARRY HERSCHER and JUSTIN J. STEIN, Am. J. Roentgenol. **43**:74 (Jan.) 1940.

The authors present a case of Albers-Shönberg disease (marble bones) associated, coincidentally, they feel, with Hodgkin's disease. The relation of the former disease to fluorine intoxication is discussed, as this produces somewhat similar changes in the bones. The authors believe that the two conditions differ in that the excessive calcification resulting from fluorine intoxication frequently extends into the adjacent soft tissues. Furthermore, there are well defined differences in histologic structure.

Although the cause of Albers-Shönberg disease is unknown, evidence points to a hereditary defect in the germ plasm carried as a mendalian recessive factor and accentuated by inbreeding. This defect apparently results in a disturbance in metabolism which affects the entire hemopoietic system. There is excessive osteoblastic activity involving the greater portion of the skeleton, if not all of it. There are associated fibrosis and enlargement of the liver, spleen and lymph nodes. Hemopoiesis is generally depressed.

SQUIRE, Chicago.

BLOOD-BORNE PYOGENIC INFECTIONS OF BONES AND JOINTS. FENWICK BEEKMAN and JOHN E. SULLIVAN, Ann. Surg. **111**:292 (Feb.) 1940.

Thirty years ago the surgeon's effort in treating this disease was to eliminate immediately the local focus from within the bone by some kind of radical procedure. In 1922 Starr showed the manner in which the infection spread outward from the metastatic focus within the metaphysis and advised early incision down to the abscess. In 1929 Orr recommended adequate drainage, packing the wound in the soft parts with petrolatum gauze and complete rest by immobilization of

the limb. In 1934 Fraser drew attention to the specific underlying condition of the acute osteomyelitis, that is, the infection in the blood stream.

This conception of the disease makes the osseous lesion merely incidental in the course of an infection of the blood stream. The authors therefore feel that more attention should be paid to the general condition of the patient and that before operation on the local lesion is undertaken the normal physiologic balance of the body should be established. The local lesions should not be drained by incision until an abscess or frank pus is found, though in cases of pyarthrosis the joint may be aspirated to relieve the tension within its capsule. Lesions due to the staphylococcus should be drained as soon as the patient's bodily condition warrants. Those due to the streptococcus can be drained when a purulent exudate has formed.

The authors give case reports to show the diminution in mortality achieved by means of the advised procedures.

BANTIN, Omaha.

MALIGNANT TUMORS OF BONE IN CHILDREN. BRADLEY L. COLEY and RICHARD L. PETERSON, J. Pediat. **15**:327 (Sept.) 1939.

Bone sarcoma in its various forms shows a distinct predilection for children and young adults. Early recognition is of the utmost importance to proper treatment. Pain is the first symptom and may precede any physical evidence of tumor by many months. Roentgen examination, determination of the blood phosphatase level and biopsy are indispensable aids in diagnosis. The portion of bone in which a primary tumor originates is often a valuable guide to the type present. Osteogenic sarcoma usually commences in the metaphysial region, endothelioma in the diaphysis, giant cell tumor in cancellous bone near the articulation and bone cyst on the shaft side of the epiphysial line. Coley and Peterson have been unable to obtain permanent or lasting regression of bone tumors by roentgen or radium treatment. They do, however, recommend a short, intensive course of fractional dose irradiation before amputation. Amputation, if the lesion is operable, should follow promptly after this treatment is completed.

RAUH, Cincinnati.

OSTEITIS FIBROSA CYSTICA GENERALISATA AND PARATHYROID TUMOUR. J. F. HUGHES, M. J. Australia **2**:830 (Dec. 2) 1939.

The author reports a case and reviews the literature on this disease. The problems of etiology, symptomatology, differential diagnosis and treatment are thoroughly discussed.

GONCE, Madison, Wis.

Diseases of the Eye

CONGENITAL ABDUCENS PARALYSIS. C. APPLE, Am. J. Ophth. **22**:169 (Feb.) 1939.

Apple reviews paralysis of the abducens nerve as to cause, preponderance on the left side and important objective findings, namely, restriction of abduction, restriction of adduction, retraction, oblique upward and downward movements, protraction, convergence insufficiency and torsion movements. He reports 3 cases from a total of 15 observed at the ophthalmic clinic of the University of Illinois College of Medicine in the past ten years. The patients in these 3 cases were personally observed and operated on to determine the underlying anatomic condition and to correct the strabismus.

W. S. REESE, Philadelphia. [ARCH. OPHTH.]

INFANTILE DACRYOCYSTITIS TREATED BY SURGICAL DIATHERMY. A. M. MACGILLIVRAY, Brit. J. Ophth. **23**:630 (Sept.) 1939.

In cases of intractable dacryocystitis in infants, MacGillivray used diathermy, with the current adjusted to an adequate cauterizing strength. With the patient under chloroform anesthesia the sac is laid bare, as in extirpation of the sac, the

incision passing through the fistula. The wound is packed with a pledget of wool soaked with epinephrine hydrochloride. The indifferent electrode is placed under the bare buttocks of the child. The current is sent through a blunt-pointed probe. After removal of the pledget the interior of the sac is thoroughly cauterized, including the infundibulum and the entrance of the nasal duct into the nose. The divided halves of the fistula are cauterized. No stitches are required. The wound heals by granulation.

W. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

NOTE ON PHLYCTENULAR OPHTHALMIA. JAMES BARRETT, Brit. J. Ophth. **23**:669 (Oct.) 1939.

Barrett states that tuberculous disease in Victoria, Australia, has been markedly lessened but that phlyctenular disease has declined to a much greater extent. This may be due to better conditions and greater care taken to avoid infection, but it may also be the expression of a biologic process of elimination. Furthermore, if the current view is taken, both tuberculous and phlyctenular ophthalmia may be due to malnutrition and may not be directly associated.

Two questions arise: 1. Is the fact that a reaction to tuberculin is obtained in cases of phlyctenular ophthalmia and of other types of ophthalmia a certain indication that the cause of the condition is tuberculous? 2. May not both tuberculous and phlyctenular ophthalmia be products of malnutrition?

W. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

INFILTRATION ANESTHESIA IN A CASE OF ACUTE GLAUCOMA. E. BLANC, Bull. Soc. d'opht. de Paris **50**:66 (Jan.) 1939.

A boy of 10 years was struck in the right eye by a ball. At the time of injury the pain was slight, but forty-eight hours later, at night, it became severe. There was a massive fresh hemorrhage in the anterior chamber. Good perception and projection of light were maintained. The raised intraocular tension did not respond to miotics during a period of five days. Ten cubic centimeters of a 1 per cent solution of procaine hydrochloride was injected into the stellate ganglion. In a few minutes there was relief from pain and inflammation. The tension was reduced from 80 to 40 mm. of mercury. The hemorrhage absorbed slowly, but vision returned to counting of fingers only. A second injection produced a Horner's syndrome after two or three minutes. Vision returned to one-half, the tension was 18 mm. and the visual field became normal. The report is of a single incident and is to be considered as preliminary. Blanc believes the procedure is useful in ocular therapeutics but should not be recommended as a panacea.

L. L. MAYER, Chicago. [ARCH. OPHTH.]

MEGALOCORNEA IN CONNECTION WITH OTHER PHYSICAL IRREGULARITIES IN MEMBERS OF THE SAME FAMILY: REPORT OF CASES. R. G. POSTHUMUS, Klin. Monatsbl. f. Augenh. **102**:1 (Jan.) 1939.

Posthumus reports 3 cases of megalocornea in a family two previous generations of which had been free from this disease. He found diabetes, labyrinthine deafness and nephritis in several members of this family; the hair was poorly pigmented, especially in the men. Extraction of a nuclear cataract in 1 adult is described, vision of 8/10 being obtained. In none of these patients with megalocornea was the globe enlarged; atrophy of the vitreous and degeneration of the pigment of the iris occurred. Typical receding of the forehead was noted in some of these patients, but this symptom cannot be regarded with certainty as hereditary. Slight mental debility of these patients cannot be evaluated reliably from a psychic or physical standpoint.

K. L. STOLL, Cincinnati. [ARCH. OPHTH.]

TREATMENT OF RETINITIS PIGMENTOSA WITH INTRAMUSCULAR INJECTIONS OF COD LIVER OIL. V. FILATOV and E. VERBITZKAYA, Vestnik oftal. **14**:21, 1939.

Six patients suffering from retinitis pigmentosa were treated with intramuscular injections of pasteurized cod liver oil. In 3 patients the injections produced a marked and quick improvement of the function of the retina, disappearance of the night blindness and improvement of dark adaptation, visual fields and visual acuity. In 2 patients the treatment yielded moderate results, and in 1 there was no improvement. Though the period of observation was short (from one to four months), the authors think it worth while to try this treatment on a large number of patients.

Filatov believes that the action of the cod liver oil depends not only on vitamin A but on the products of disintegrated liver tissue. In order to verify this, two small pieces of conserved human liver were implanted under the skin of a patient with retinitis pigmentosa. The vision improved from 0.3 to 0.4, the visual fields increased about 10 degrees and the dark adaptation improved. The histories and visual fields of the patients are presented in the article.

O. SITCHEVSKA, New York. [ARCH. OPHTH.]

BLUE SCLERA. H. L. JENSEN and K. K. ORTMANN, Ugesk. f. læger **101**:275 (March) 1939.

Jensen and Ortmann, reporting 2 cases of Lobstein-Eddow disease, osteopsathyrosis idiopathica, state that in the disorder blue scleras, a tendency to fractures and otosclerosis constitute a triad. As seen in their second case, blue scleras are not always accompanied by the tendency to fractures. There is generally a proportionality between the degree of coloring and this tendency. All authors agree that blue scleras are the dominating symptom. The color has been observed in 5 generations and established in 50 descendants of 1 person. A certain intensity of the coloring, a familial character and the combination of osseous and auditive stigmas in at least 1 member of the family are necessary for a positive diagnosis. The abnormal fragility of the bones depends on insufficient periosteal ossification coincident with inability of the bone tissue to take up calcium. The patients may become greatly deformed; in cases of extreme involvement they are referred to as "men of glass." The underlying cause of the symptom complex is unknown. While in 1 family the disorder has appeared only in 20 male members, as a rule both men and women are affected. Transmission is probably dominant. The disorder may skip several generations, to reappear as the result of exogenic (disease) or endogenic factors (puberty or gravidity).

J. A. M. A.

Skin Diseases; Allergy

OBSERVATIONS ON TOTAL WATER AND SODIUM EXCHANGES IN ASTHMATIC PATIENTS. JOHN SHELDON, HOMER HOWES and GEORGE STUART, J. Allergy **11**:1 (Nov.) 1939.

Experiments were conducted on 5 patients in whom the asthmatic attack could be controlled. In 3 the attack could be initiated by the ingestion of foods and in 2 by the inhalation of pollen. The salt and the water metabolism were studied.

The authors concluded that there was a definite loss of body water associated with asthma of at least twenty-four hours' duration. Urinary sodium was increased during a prolonged asthmatic attack. The total heat production during an attack was not measurably increased, so that the loss in body weight that occurred was due to loss of body water.

HOYER, Cincinnati.

TIME REQUIRED FOR THE PRODUCTION OF HAY FEVER BY A NEWLY ENCOUNTERED POLLEN, SUGAR BEET. E. W. PHILLIPS, J. Allergy **11**:28 (Nov.) 1939.

A new industry was introduced in the area around Phoenix, Arizona, in 1936, that of raising sugar beets for seed. The plants are from 3 to 6 feet (91.44 to 182.88 cm.) high, bloom in April and May and produce an abundance of pollen. A few patients with hay fever who were sensitive to the pollen were observed in

1937. The number increased greatly in 1938. This may have been due, to some extent at least, to the great increase in the number of acres planted, from 1,800 acres in 1936 to 5,500 in 1938.

The author feels that two years of seasonal contact with the pollen was required to produce clinical evidence of sensitivity.

Persons sensitive to the pollen of other chenopods seemed to be sensitive to the beet pollen. It has a specific reagin of its own, since extracts of pollen of amaranth and Russian thistle did not protect the person against the sugar beet. Injections of an extract of sugar beet pollen, however, did give relief.

HOYER, Cincinnati.

THE TRANSFERENCE OF REAGINS IN BLOOD TRANSFUSIONS. W. P. GARVER, J. Allergy **11**:32 (Nov.) 1939.

Three cases are reported in which the skin of a nonsensitive person became passively sensitized as the result of a transfusion of blood from a sensitive donor. Clinical sensitivity was not demonstrated in any of these cases.

HOYER, Cincinnati.

IMMUNOLOGIC RELATIONSHIPS BETWEEN COW'S MILK AND GOAT'S MILK. LEWIS WEBB HILL, J. Pediat. **15**:157 (Aug.) 1939.

It has been definitely established by several investigators that cow and goat casein are immunologically almost identical. The question whether the lactalbumin of cow's and that of goat's milk are immunologically distinct has never been definitely answered. Forty-four eczematous infants with positive intracutaneous reactions to cow lactalbumin were tested with goat lactalbumin. Ten gave negative reactions, 9 gave doubtful reactions and 25 gave positive reactions. From these reactions it appears that the species specificity of cow and goat lactalbumin is not great.

Proteins from closely related species often do not show great specificity, particularly if the protein has the same specialized function in each species. There are many antigens the specificity of which is determined by chemical constitution and function rather than by species.

Hill cites the theory that many antigens contain two sensitizing determinants—one species specific and another common to the antigen in question and to other closely related antigens as well—and that a person may become sensitized to the species-specific factor alone or to both determinants.

The eczematous infants on whom the tests with lactalbumin were made are used as an example to bear out this theory. Some were sensitized to the species-specific factor of cow lactalbumin alone and some also to the factor common to both cow and goat lactalbumin; in either of these two groups there may be sensitization to casein as well. In still a third, but much smaller, group there may be sensitization to casein alone. Goat's milk is indicated as a therapeutic agent only for the first group.

Hill continues his paper with a discussion of a group of infants with severe hypersensitivity to cow's milk, as a rule without eczema, who go into alarming collapse on the administration of only small amounts of cow's milk and who can take goat's milk with impunity. In these infants there is no sensitivity to casein, but there is sensitivity to the species-specific determinant of cow lactalbumin alone.

RAUH, Cincinnati.

DESQUAMATIVE ERYTHRODERMA OF INFANTS, WITH SPECIAL REFERENCE TO LEINER-MOUSSOUS DISEASE. P. LEREBOULLET, Progrès méd. **67**:946 (July 1) 1939.

Lereboullet points out that the desquamating erythroderma usually designated as Leiner's disease was described by Moussous in France some years before Leiner's classic description appeared. In contrast to Leiner's opinion, the author does not feel that infants showing this condition should be taken off the breast. It seems to him that a satisfactory explanation of the condition has not been

reached, although the infants whom he observed showed a high incidence of enterococci both in the stools and in scales from the skin. Conservation measures with attention to hygiene and a relatively low fat diet if the infant is artificially fed are advocated.

LESLIE, Evanston, Ill.

SHOULD CONGENITAL HEMANGIOMA COME TO OPERATION IN INFANCY? MAERZ, München. med. Wchnschr. **86**:1356 (Sept. 1) 1939.

Hemangiomas in infants grow rapidly. Satisfactory removal becomes more difficult the longer one waits and the larger the tumor becomes. The treatment of choice is application of radium. If this is not available, surgical removal is indicated.

For the flat angiomas (naevus flammeus) radium therapy is not satisfactory and surgical removal, if technically possible, may be indicated. The pale angioma frequently found on the back of the neck disappears spontaneously.

BRAHDY, Mount Vernon, N. Y.

Surgery and Orthopedics

INDICATIONS FOR THE SURGICAL LIGATION OF A PATENT DUCTUS ARTERIOSUS. JOHN P. HUBBARD, PAUL W. EMERSON and HYMAN GREEN, New England J. Med. **221**:481 (Sept. 28) 1939.

The introduction of a successful method of ligating the ductus arteriosus calls for a critical analysis of the indications for such surgical intervention. The authors analyze and discuss the indications for operation in the 1,000 cases of congenital malformation of the heart collected from the literature by Abbott and also in the cases described in other similar studies.

In a patient with patent ductus arteriosus, retardation of growth, signs of aortic regurgitation or evidence of cardiac insufficiency should suggest a shunt large enough to throw an excessive burden on the heart and should serve as an indication for ligation of the ductus.

Ligation of a patent ductus may lessen or altogether remove the danger of the development of subacute bacterial endarteritis, but to date there is no proof of this. Final judgment in this regard should be withheld until more is known of the surgical risk and until it has been shown by years of observation that a ligated ductus remains free of this complication.

GENGENBACH, Denver. [FROM AUTHORS' SUMMARY.]

IMPROVED SPINAL ANAESTHESIA. GRAHAM MACPHERSON, Brit. J. Surg. **27**:34 (July) 1939.

The author outlines his careful technic for spinal anesthesia and recommends the use of nupercaine. He reviews important papers on the subject and draws conclusions from these and from a study of over 500 cases of his own. He associates himself with those surgeons who so ardently support the wider adoption of spinal anesthesia.

KEITH, Toronto, Ontario.

Teeth and Dentistry

CALCIUM METABOLISM AND TEETH. RUDOLF KRONFELD, Mil. Surgeon **86**:250 (March) 1940.

In summarizing present day knowledge of this subject, Kronfeld states:

". . . attempts to improve the structure of erupted teeth by means of calcium and phosphorus or vitamin preparations are useless. Even if the calcium were assimilated by the body there is no way in which it could be incorporated into the enamel of fully formed erupted teeth.

"The important period for the structure and composition of the enamel of the permanent teeth is from birth to the age of five or six years. Especially significant with respect to the first permanent molars are the first two years of life. During this formative period a diet well fortified in the necessary building elements is essential for strong, well built teeth. The best natural source of calcium is milk. Vitamin D, which is necessary for the proper assimilation of calcium by the body, is found in milk, butter, egg yolk, cod liver oil and other fats; if necessary it can be supplemented in the form of vitamin D concentrates.

"Once the teeth have erupted they have just as good or just as bad a structure as they are going to have for the rest of their life.

"There is no conclusive statistical evidence that the incidence of caries during pregnancy is greater than the incidence in non-pregnant women of corresponding age. . . . there is no evidence of calcium withdrawal from the mother's teeth."

SANFORD, Chicago.

THE ECONOMIC STATUS OF THE COMMUNITY AND THE DENTAL PROBLEM OF SCHOOL CHILDREN. H. KLEIN, Pub. Health Rep. **55**:187 (Feb. 2) 1940.

This report is of 40 urban communities embracing 200,000 children. The evidence available seems to indicate that the intrinsic tendency of the child to experience attacks on the permanent teeth does not depend on the economic status of the community in which the child lives. The volume of dental care in the form of fillings in the permanent teeth increases markedly with rise in the economic level of the community. The odontothanatotic rate (the number of permanent teeth extracted and indicated for extraction per hundred children) diminishes as the economic level of the community rises.

SANFORD, Chicago.

Miscellaneous

GRANULOCYTOPENIA IN SULFAPYRIDINE THERAPY. VERA B. DOLGOPOL and HAROLD M. HOBART, J. A. M. A. **113**:1012 (Sept. 9) 1939.

In reviewing the literature the authors found 3 cases of granulocytopenia and several of leukopenia after sulfapyridine therapy. All the patients were infants treated for pertussis and pneumonia. In the 1 fatal case there were complete disappearance of granulocytes and an aplastic marrow.

They advise biweekly blood counts during sulfapyridine therapy and for two weeks after withdrawal of the drug. The conditions in these cases always occurred when large doses were used over long periods.

HEERSMA, Kalamazoo, Mich.

RENAL COMPLICATION IN SULFAPYRIDINE THERAPY. Y. F. TSAO, MARY E. MCCRACKEN, J. CHEN, P. T. KUO and C. L. DALE, J. A. M. A. **113**:1316 (Sept. 30) 1939.

Among 40 Chinese children treated with sulfapyridine, 5 showed hematuria. All were suffering from malnutrition and avitaminosis. One died of uremia resulting from obstruction by uroliths in the ureter. The authors feel that children are more susceptible to renal complication accompanying sulfapyridine therapy than are adults and that such complications may occur in association with any urinary acidity.

HEERSMA, Kalamazoo, Mich.

A BEDSIDE TEST FOR SULFAPYRIDINE. HERMAN D. RATISH and JESSE G. M. BULLOWA, J. Lab. & Clin. Med. **25**:654 (March) 1940.

The technic for the test is given in detail. It is dependent on the ether extraction of sulfapyridine from the blood. It may be performed in ten minutes with simple glassware and reagents.

READING, Galveston, Tex.

ATROPINE INTOXICATION: ITS MANIFESTATIONS IN INFANTS AND CHILDREN. HENRY G. MORTON, J. Pediat. **14**:755 (June) 1939.

Belladonna and its derivatives are widely used in pediatrics. Symptoms of atropine intoxication occasionally occur. They are often unrecognized as related to the administration of the drugs, and death may result. From 1930 to 1938, 8 instances of atropine poisoning, in 2 of which death resulted, occurred among 3,200 patients admitted to the pediatric department of the Duke Hospital. These 8 cases are reported. Morton discusses the action of the drug, the toxic manifestations and treatment of the intoxication. RAUH, Cincinnati.

OVER-REGIMENTATION IN PEDIATRICS. H. KENNEDY JR., South. M. J. **33**:50 (Jan.) 1940.

Kennedy states the belief that the chief problem before the pediatrician today is a diminution in regimentation and the avoidance of an increase in his physiologic problems.

"Let the baby have some individuality," he says, "and, therefore, a more stable character." F. W. SCHLUTZ, Chicago.

THE CONCENTRATION OF SULPHANILAMIDE IN THE SALIVA FOLLOWING ORAL ADMINISTRATION. S. WILLIAMS, B. SPLATT and R. JAKOBOWICZ, M. J. Australia **1**:120 (Jan. 27) 1940.

In 7 patients the concentration of sulfanilamide in the saliva bore no constant relation to the concentration of the drug in the blood. Sulfanilamide caused neither stimulation nor inhibition of the salivary glands as judged by the volume of saliva excreted and the concentration of urea in it. Single doses of sulfanilamide up to 4 Gm. sometimes failed to cause any significant excretion of the drug into the saliva, whereas single doses of 6 Gm. given with large quantities of water by a Rehfuss tube caused prolonged excretion in the saliva. GONCE, Madison, Wis.

Society Transactions

ARGENTINE PEDIATRIC SOCIETY

ALEJANDRO M. OYUELA, M.D., *President*

JOSÉ F. MORANO BRANDI, M.D., *Secretary*

Annual Meeting, LaPlata, Argentine, Sept. 21-23, 1939

The Epidemiologic Factor in the Genesis of Tuberculosis in Childhood. DR. FAUSTO C. TUCCI, Buenos Aires.

By taking into account the laws of Bernard and Debré, which refer to the factors favoring tuberculous infection, it has been possible to analyze the sources of intradomiciliar, familial or extrafamilial contagion, of infection in schools—especially private schools—public places, institutions and hospitals and of contamination of animal origin, principally bovine. In regard to the latter, mention should be made of the statistics collected by Dr. Angela M. de Soriano, who discovered the tubercle bacillus in 45.5 per cent of the raw milk examined, in 56.2 per cent of the cream and in 23.9 per cent of the pasteurized milk sold in the city of Buenos Aires.

Statistics from the Packing-House Division of the Ministry of Agriculture, compiled during the five year period from 1934 to 1938, show that 7.3 per cent of the cattle and 15.67 per cent of the pigs had generalized or localized tuberculosis. The statistics of Petit in Paris and of Eber and others in Germany supply information with regard to infection in domestic carnivores, such as cats and dogs. The publications of Dr. Anibal Da Grana, of Argentina, also give information concernnig the frequency of tuberculosis in dogs and cats. With regard to tuberculosis of avian origin, according to the statistics of Prof. Alfredo Fontana, of the University of Milan, of 75,000,000 domestic fowls in Germany, about 7,500,000 (10 per cent) are tuberculous and up to 90 per cent of the old hens are infected with the tubercle bacillus.

A helpful filing card has been used in collecting statistical information for the epidemiologic survey in the tuberculosis service of the Children's Hospital of Buenos Aires. Of 1,448 tuberculin-positive children studied personally during 1936 and 1937, more than half, or 50.96 per cent, had a tuberculous infection of unknown origin.

Prophylaxis of Tuberculosis in Childhood. PROF. J. C. RECALDE CUESTAS, and DR. FRANCISCO ROSELLO and DR. ANGEL INVALDI, Rosario.

We believe, with Alfaro, Pehu and Dufourt, that the whole problem of antituberculous prophylaxis reduces itself almost entirely to the protection of children, during infancy and, principally, during the first few years of childhood.

In discussing the problem of prophylaxis of infantile tuberculosis, these points must be considered: (1) contagion (including reinfection), (2) vaccination and (3) general economic and hygienic conditions.

In order to avoid contagion, principally in the home, which is the more serious the younger the child, one should proceed with prenatal prophylaxis, the immediate separation of the newborn infant from the tuberculous mother and the preservation of the child, especially the nursling, from the danger of infection by the isolation and treatment of any member of the family with the disease. The early examinations of the child should be made in the milk station dispensaries in early infancy and at school age; the child should be classified as suspected of

being infected or sound and should be vaccinated with BCG vaccine. Examinations of adults should be carried out in antituberculosis dispensaries and in the preventive clinics in the workmen's quarters which are organized for periodic examination of presumably healthy persons. In addition, adequate propaganda should be directed toward pointing out to every healthy person the desirability of submitting to a medical examination.

With respect to the child of school age, the inquiry should be initiated by establishing the obligation of every person to supply data for the "Health Card," which should include information about the results of tuberculin tests and roentgenographic examinations (Recalde Cuestas-Chiodin model, approved by the third Provincial Children's Convention at Santa Fe).

For proper isolation, appropriate institutions, such as maternity hospitals for the tuberculous mother (crèche Landouzy), are indispensable; the nursling may often be placed in homes (as suggested by Grancher's work). As auxiliary mediums, schools for weak children, summer camps, preventoriums, etc., are useful. The isolation and treatment of infected adults should be effected by making available a sufficient number of beds, since it is a well proved fact that in the investigation to locate the source of contagion in a child, one often finds an adult to be responsible, especially when the infection is severe.

None of the criticisms made of vaccination with BCG vaccine have invalidated the analysis of results from vaccination that Calmette and his school have made. BCG vaccine has been used in many different countries via the digestive tract. Of 443,656 children vaccinated in 46 different countries, not including France, the general rate of infant mortality between birth and 1 year of age from all causes has been 7.9 per cent for the vaccinated and for those not vaccinated 15.3 per cent, or about 50 per cent less in those vaccinated.

With respect to the experience with BCG vaccine in the region along the Plate River, the conclusions of Dr. Alejandro Raimondi, of Buenos Aires may be cited:

In more than 56,000 vaccinated children, there has never been observed any contraindication, intolerance or reaction of any type. The advantages of vaccination are more definite when the vaccine is given subcutaneously. The child vaccinated with BCG who does not react distinctly to tuberculin at 6 months of age should be vaccinated again.

The conclusions of Professor Sayago and Drs. Chattas, Naput and DeGoy, of Córdoba, Argentina, are as follows: General mortality among 1,733 children vaccinated up to Nov. 30, 1938 has been found to be 8.3 per cent, as compared to 15.6 per cent among children not vaccinated.

Dr. Pedro Cantonnet Blanchi, of Uruguay, in commenting on his experience since 1930 and the results obtained in his country among 50,000 vaccinated children, 77 per cent of whom were given the vaccine by mouth and the rest subcutaneously, stated: Following oral administration of the vaccine, a late, inconstant allergic reaction was obtained, but it was intense and transient, being lost in 80 per cent of the patients before a year. An allergic reaction was manifest in only 9 per cent of the entire series and in only 1.1 per cent of those who were revaccinated.

The subcutaneous use of the vaccine also had its inconveniences, since it caused nodules and abscesses and the allergic reaction was lost in 54 per cent of the patients in a year.

The incidence of tuberculosis (38 per cent) and the mortality (6 per cent) were identical in vaccinated and in nonvaccinated persons.

Poverty, ignorance and unhealthful living quarters cannot be eliminated from any considerations concerning community health. In consequence, the prophylaxis of tuberculosis in general and in childhood in particular is a deep responsibility of the government that the state itself should face with all its energy, in a wholehearted manner, with ample resources and appropriate legislation.

The prophylaxis of tuberculosis in childhood, which is inseparable from the general prophylaxis of tuberculosis, demands bringing into play all direct and indirect measures for endeavoring to get the susceptible child into a state of

defense against the tubercle bacillus; he should be made allergic to tubercle bacilli through vaccination with BCG vaccine and given all the aids to health and hygienic living.

Tuberculosis is a national danger. It should be combated with federal weapons and the government should arrange economic resources and necessary legal aid to orient and coordinate official powers as well as private endeavor throughout the republic.

Considerations of the Treatment of Pulmonary Tuberculosis in Childhood by Gaseous Collapse Therapy. Dr. Fausto C. Tucci, Buenos Aires.

Pneumothorax in early infancy and even in childhood, up to the age of puberty, constitutes an exceptional procedure and is indicated only for treatment of grave primary disease processes which tend toward caseation or of primary tuberculosis. However, there is a certain amount of skepticism about the success of collapse therapy even for these conditions, in view of the fact that they are dense disease processes, that lungs affected by them are poorly compressible and that they are nearly always accompanied by marked caseous glandular reactions as well as by dissemination and early symphysis which make difficult and hinder the successful carrying out of pneumotherapy. On the other hand, it is an accepted mode of therapy for the infiltrative, exudative, caseous subsecondary forms (hematogenous tuberculosis) and for caseous pneumonia with necrotic foci.

Pneumothorax is indicated only in primary or secondary infiltrations, splenopneumonias or epituberculosis and only in the rare case, certainly, in which the congestive or inflammatory processes show unfavorable evolution toward softening (progressive, focal, intrapulmonary tuberculosis), a circumstance that is found only exceptionally. I believe, on the other hand, that pneumothorax is definitely indicated in exudative, caseous and ulcerative processes in children at the age of puberty and in adolescence and in those forms of reinfection which are of the anatomicoclinical type of infiltration of Assmann or that of Redeker, also called infraclavicular infiltration, juvenile infiltration or prephthisic infiltration, and the forms engendered by it. It is known today that this anatomicoclinical variety represents the most common of the parenchymatous forms of superinfection of the tertiary type. Assmann and Redeker consider the early infiltration a lesion peculiar to adolescence and youth, that often produces a roentgenographic picture which is surprising.

Children tolerate pneumothorax admirably; it can be practiced as an ambulatory procedure, without inconvenience, according to my personal experience, but it is in particular the ideal and elective procedure for hospitalized children. As examples, I cite the results obtained in 6 patients between 10 and 13 years of age, ill with severe tuberculosis, that is, with caseous pneumonic cavities, who were treated in my service at the Children's Hospital of Buenos Aires by gaseous collapse therapy and cured within twelve months (3 patients), fourteen months (1 patient) and sixteen months (2 patients). They were clinically, bacteriologically, roentgenographically (with or without defect) and biohumorally cured. Roentgenograms were taken of each patient before, during and after treatment. I have arrived at the following conclusions:

Therapeutic pneumothorax constitutes the only efficient treatment and gives unquestionable results in grave, caseous tuberculosis of childhood and puberty, whether the infection is subsecondary (bronchogenic or hematogenic phthisis) or is a tertiary form with early infiltration or is an evolutionary form.

Bilateral lesions are no contraindication. My experience permits me to assert that in many cases pneumothorax acts contralaterally without the necessity of resorting to bilateral pneumothorax simultaneously or successively.

The lack of beds for tuberculous patients constitutes a veritable medicosocial national problem, and the necessity of practicing ambulatory pneumothorax often arises; such therapy permits of as good results as when treatment is carried out in hospitals or sanatoriums, provided always that it is in charge of medical specialists with thorough knowledge of the method.

The duration of collapse therapy in childhood and puberty merits special interest because of the gravity of the lesions at those ages; the rapidity of extension of the disease process is governed by special physiologic factors in the immunobiologic reactions of each patient and depends, in great part, on how early the diagnosis is made. In all the patients treated the disease is shorter than in the adult, because the lesions are fresh, the tissues are more elastic and, consequently, they are easier to repair. In spite of the results I have obtained, I am not able to fix a general normal for the duration of pneumothorax during childhood and puberty, since it is necessary to appraise each patient individually, as in each there is a different series of factors at work.

Bovine Type of Koch Bacillus in Tuberculosis of Childhood. Dr. Eduardo G. Casselli, Dr. C. B. Teobaldo and Dr. Alfredo Actis Dato, La Plata.

Attention should be called to human contagion of tuberculosis of animal origin, especially through dairy products. One must mention the statistics of Simon and Redeker, who found that in Germany from 41 to 50 per cent of tuberculosis of the bones and of the glands was of the bovine type and that in England and Scotland the proportion was up to 90 per cent. There are other means of contagion from animals, such as from pigs, milk of goats, from mules and from such domestic animals as dogs, cats, parrots and other birds. The percentage of tuberculosis of bovine origin in the nursling has been recorded in different countries, and prophylactic measures have been taken by the governments of England and the United States in regard to cows that are tuberculous or are tuberculin-positive.

In the Republic of Argentina there exist no statistics about childhood tuberculosis of bovine origin and, as far as tuberculosis of cattle is concerned, we are in full accord with the words of Dr. Francisco Rosenbusch, who has said that the proportion of tuberculosis on the country farms far from the centers of population is low but that in the dairy herds from 50 to 80 per cent of the cows react positively to tuberculin.

As the result of an investigation carried out during the first six months of 1939, of 602,981 cattle in the slaughter yards of Liniers, Argentina, 3,903, or 0.56 per cent, were confiscated because of tuberculous lesions; of 208,591 pigs, 8,499, or 4 per cent, were destroyed because of tuberculous lesions of bovine bacillary origin, due to feeding with milk from infected cows.

Many investigators have studied the frequency of tuberculous meningitis of children caused by the bovine type of tubercle bacillus, and mention should be made of the publications of Lesne, Sáenz, Salembier and Costil in France, Park and Montanus in North America, Moellers and Lange in Germany and Griffith, Gobbert and Eastwood in England. According to the statistics of Park and Krumwide, in the child glandular, osteoarticular, peritoneal and meningeal localizations are the lesions most frequently caused by the bovine type of tubercle bacillus.

We had the opportunity to study a case of infection in childhood with the bovine type of tubercle bacillus. A boy whose diet in Lithuania for several years had consisted mainly of raw cow's milk was admitted to the Children's Hospital of La Plata with tuberculous peritonitis of the fibrocaseous type. One month later, bacillary meningitis developed, the tubercle bacillus being found in the cerebrospinal fluid. No history existed of tuberculosis in his immediate family or in the immediate vicinity. Roentgenograms of the thorax were normal. The presence of the human type of tubercle bacllus was confirmed by a bacteriologic examination of the cerebrospinal fluid, positive cultures on the mediums of Loewenstein and Petragnani, intraglandular inoculations of guinea pigs and by the isolation and differentiation of the bacillus from abdominal glands of the patient.

As the patient studied had peritoneal and meningeal manifestations and apparently his lungs were undamaged, according to the normal-appearing roentgenograms, we believed it interesting to investigate in him the possible presence of the bovine type of tubercle bacillus, as he had been fed on raw cow's milk for seven years and particularly since it is considered that tuberculosis of the child

produced by the bovine type of tubercle bacillus is due to the ingestion of raw milk and its products.

In spite of the fact that all the possibilities mentioned as being common in contagion by the bovine type of tubercle bacillus in childhood were present in this case, such as (*a*) negative history of tuberculosis in family and environment, (*b*) ingestion of raw cow's milk in massive quantities for seven years, (*c*) admission to the hospital with a complete picture of tuberculous peritonitis, (*d*) clinical and roentgen examination of the respiratory apparatus which showed no apparent abnormality, although one cannot be certain of this because no anatomic-pathologic study of the lung was made, and (*e*) death shortly of tuberculous meningitis, (*f*) results of bacteriologic, cultural, differential and experimental study were positive for the human type of tubercle bacillus.

Person to person contamination is the form most common, and its elimination should be an essential part of prophylaxis as far as control of contagion in childhood tuberculosis is concerned.

Infection by the bovine type of tubercle bacillus should be taken into account as long as statistics reveal that there exist patients with tuberculosis of bovine bacillary origin. It is indispensable to control the vaccination of cattle and especially to supervise the production of milk and milk products that are used in feeding the child.

Mortality from Tuberculosis in the Republic of Argentina: With Special Reference to Infant Mortality. Dr. Pedro L. Luque, Córdoba, Argentina.

Argentina loses 14,000 lives annually from tuberculosis, or 11.2 inhabitants of each 10,000. This rate was 13.4 per 10,000 a quarter of a century ago.

The figures for mortality from tuberculosis in different regions of the country in 1934 and 1935 were higher for the extreme north (196 per 100,000 inhabitants in Jujuy and 162 in Salta) and lower for the rest of the states and territories.

In 1914 to 1915 the highest rates were in the coastal and central states, the same as in the city of Buenos Aires. This shifting of the zone of highest mortality may be explained on the basis of what Sayé calls the stage of pretuberculization and the one subsequent, frank tuberculization.

Mortality from tuberculosis varies in the different age groups. Two well marked apexes may be placed in relief: One comprises the first year of life and the other falls in full youth in towns of recent tuberculization; the peak mortality is in the period from maturity up to old age in the regions that are in the stage of detuberculization.

In the city of Buenos Aires the mortality from tuberculosis reached in 1936 the level of 14.5 for each 10,000 inhabitants in the first year of life, descending below 4 in those between 5 and 15 years of age and again increasing among those beyond that age, reaching its highest figure among persons between 20 and 30 years of age with the rate of 19.3, at which point a slow descent began that for those more than 60 years of age was transformed into a sharp drop.

Mortality from tuberculosis represents not more than 0.9 per cent of the total deaths among inhabitants in the first year of life.

There do not exist great differences between the mortality from tuberculosis in boys and in girls up to the age of 5 years, but after that age the predominance of mortality in girls is manifest, the rate being almost double that in boys at puberty.

The different clinical forms of tuberculosis of infants demonstrate that the younger the person, the more difficult it is to localize his illness. Generalized tuberculosis and tuberculous meningitis predominate in the early years but later give place to the more localized forms and, above all, to pulmonary tuberculosis.

Pathobiomorphologic Diagnosis of Intrathoracic Tuberculosis in Childhood. Dr. Fausto C. Tucci, Buenos Aires.

My opinions do not differ fundamentally from the concept of Ranke and from the theories of Petruschy, Schulz, Hamburger, Widowitz, Aschoff, Puhl and Beitze,

Liebermeister, Hollo, Schurmann and Dietl, which do not deviate substantially from Ranke's original ideas. On the basis of long experience, I have conceived a classification of infantile tuberculosis that serves a practical and useful purpose in the complex organization of the dispensary and one which permits a rapid interpretation of each case from the pathogenic, anatomic, clinical and roentgenographic standpoint.

Tuberculosis may be divided into two great groups: (*a*) tuberculosis of primary infection and (*b*) tuberculosis of superinfection.

The first comprises all those forms that develop from the fixation of the tubercle bacillus in the organism until the primary, sclerogenous allergic reaction (Ranke) is established. This first group is further divided into primary, subprimary and postprimary forms. The primary forms are the anatomic roentgenographic varieties, typical of the commencement of the primary infection. The subprimary forms are those that present themselves as isolated lesions or accompany or even follow closely the primary forms. The postprimary forms are the sequelae of the two preceding forms.

The second group, tuberculosis of superinfection, comprises: (*a*) secondary forms—congestive, inflammatory modalities or simple, perifocal, benign and regressive exudates; (*b*) subsecondary forms—those that occur isolatedly or follow closely after the secondary forms; (*c*) postsecondary forms—the sequelae of the two preceding forms.

Tertiary forms are those of chronic tuberculosis or fibroulcerative tuberculosis.

My classification in outline form follows:

1. Tuberculosis of primary infection
   - A. Primary forms:
     - (1) Primary diffuse infiltration
     - (2) Soft primary complex. Caseous lobular pneumonia
     - (3) Primary tuberculosis; caseous pneumonia with limited focus: early isolated cavern
   - B. Subprimary forms: varieties that can be isolated, accompany or follow closely the primary forms
     - (1) Tumorous inflammatory adenopathy
     - (2) Tumorous caseous adenopathy
     - (3) Early disseminations (lymphogenous, lymphohematogenous or hematogenous)
       - (a) Discrete, early, micronodular dissemination (isolated metastasis)
       - (b) Curable hematogenous dissemination
       - (c) Acute miliary tuberculosis
     - (4) Bronchogenic dissemination: tuberculous bronchopneumonia with disseminated foci
     - (5) Exudative pleurisy
       - (a) Of a great cavity
       - (b) Mediastinal
       - (c) Interlobular
       - (c) Diaphragmatic
     - (6) Perifocal reactivations
   - C. Postprimary forms: sequelae of primary and subprimary forms
     - (1) Primary calcified complex
     - (2) Calcified chancre of Ghon
     - (3) Adenopathy with calcification
     - (4) Calcified nodules (Simon, Puhl)
     - (5) Fibrotic sequelae (indurated fields)

(6) "Tramite" (Bezançon); perilobulitis (Sergent); reticulated lymphangitis (Schürmann); striation (Stürtz)
(7) Calloused periadenitis
(8) Adhesive pleurisy
  (a) Parietal: apical, marginal or laminar
  (b) Mediastinal
  (c) Interlobular
  (d) Diaphragmatic

2. Tuberculosis of superinfection (by reactivation, endogenous or exogenous reinfection)

A. Secondary forms
  (1) Perifocal infiltrations
  (2) Corticopleuritis
  (3) Perihilar infiltrations
  (4) Epituberculosis of Eliasberg and Neuland or splenic pneumonia of Grancher
  (5) Tumorous, inflammatory adenopathy

B. Subsecondary forms: varieties that can be isolated or follow closely the secondary forms
  (1) Caseous tumorous adenopathy
  (2) Focal, progressive, intrapulmonary tuberculosis
  (3) Tuberculous pneumonia with necrotic foci
  (4) Tuberculous bronchopneumonia with disseminated foci
    (a) Acute: extensive caseous or "galloping" tuberculosis
    (b) Subacute
  (5) Hematogenous disseminations
    (a) Isolated metastases
    (b) Curable disseminated hematogenous tuberculosis
    (c) Caseous hematogenous tuberculosis
    (d) Acute miliary tuberculosis
  (6) Exudative pleurisy
    (a) Of a large cavity
    (b) Mediastinal
    (c) Interlobular
    (d) Diaphragmatic

C. Postsecondary forms: sequelae of the secondary and subsecondary forms
  (1) Calcified nodules (Simon, Puhl)
  (2) Fibrous sequelae (indurated fields)
  (3) "Tramite" (Bezançon), perilobulitis (Sergent), reticulated lymphangitis (Schürmann), striation (Stürtz)
  (4) Calloused periadenitis
  (5) Adhesive pleurisy
    (a) Parietal
    (b) Mediastinal
    (c) Interlobular
    (d) Diaphragmatic

D. Tertiary forms
  (1) Early infiltrated; fibrocaseous tuberculosis (chronic tuberculosis or tertiary fibrosclerous)

(2) Localized, or lobulitis
(3) Extensive fibrocaseous, caseous tuberculosis
(4) Extensive caseous fibrocaseous tuberculosis; fibrous tuberculosis
(5) Localized or discrete tuberculosis
(6) Dense tuberculosis

Chemotherapy of Tuberculosis in Childhood. Dr. Fausto C. Tucci and Dr. Jose E. Mosquera, Buenos Aires.

We feel that in the forms of benign primary tuberculous infection it is essential to stimulate the organism in order to stir up its defenses, and for that nothing is better than tonic and antiphlogistic medication.

Encouraging results have never been obtained with gold compounds in primary tuberculous infection. Results with this form of therapy have been almost constantly negative in the grave forms of tuberculous superinfection of the subsecondary period. The benign secondary forms are systematically improved with antiphlogistic and antitoxic medication. The use of gold compounds is not justified in the postsecondary forms, because they are types in frank regression.

For tertiary tuberculosis there does not exist any treatment better than the one of unquestionable value: collapse therapy with which is used, systematically as a therapeutic help, gold salts in the smallest doses, never exceeding 0.05 Gm. weekly, by preference in the form of the suspension in oil.

We believe that gold compounds are potent medicaments and are suspicious of their disturbing action on the equilibrium of the bodily defenses; they are capable of irritating the reticuloendothelial system and especially of causing inflammatory changes, focal or visceral. Among the children that come to our service, there have been a minimal number of instances of albuminuria, a few instances of nephritides and several instances of erythroderma from the use of gold compounds.

The treatment of infantile tuberculosis has been based up to now on hygienic and dietetic measures. We believe that the morrhuates constitute a form of therapy that, when used in association with hygienic and dietetic measures, has a favorable action on the general and local state in the primary forms of tuberculosis, in superinfection, which is clinically attenuated, as well as in active forms: primary and secondary infiltrations (simple, inflammatory, congestive and perifocal varieties).

The therapeutic action of the morrhuates in the treatment of pulmonary tuberculosis in the child can be compared to that of the gold salts used in the treatment of the adult. We attribute their therapeutic action to their saponified composition and to their colloidal characteristics. They can be used by the intravenous route, which makes them more active, according to our experience, than when they are given subcutaneously or intramuscularly.

In the tertiary forms of tuberculosis we prefer the use of salts of gold as a "coadjuvant medication," not giving more than 0.05 Gm. weekly, in repeated courses three months in length, with one month of rest between each course.

A Comparative Study of the Old Tuberculin of Koch, the Esotuberculin of Finzi and the Purified Protein Derivative of Seibert and Long. Dr. Fausto C. Tucci and Dr. Jose B. Gomez, Buenos Aires.

To obtain similar epidemiologic indexes it is indispensable to work with tuberculins of equal sensitivity, adequately controlled. We used the old tuberculin of Koch, prepared by the Bacteriologic Institute of the National Department of Hygiene by a standard technic under vigorously controlled conditions. The solutions were divided into Jena glass capsules of 1 cc. capacity. The dilutions 1 to 1,000, 1 to 5,000 and 1 to 10,000 were renewed every fifteen days, and those of 1 to 100 and 1 to 10 every thirty days. We also tried the purified protein derivative of Seibert and Long and the esotuberculin of Finzi, in order to compare the results. The purified protein derivative of Seibert and Long is obtained from filtration of cultures of three species of Mycobacterium tuberculosis (human type)

grown on a synthetic medium adopted by the Bureau of Animal Industry of the United States Department of Agriculture. Finzi's esotuberculin is a polyvalent preparation made from mixed exotoxins of tubercle bacilli of both the human and the bovine type. The bacilli are grown in 5 per cent glycerinated broth at 38.5 C. for six to eight weeks. The thick film on the surface of the liquid is forced to the bottom of the vessel by means of a special pipet, and the broth is aspirated, filtered and treated with a 0.5 per cent solution of formaldehyde U. S. P. The product thus obtained can be used forty-eight hours later.

The intradermal test of Mantoux was employed because of its easy administration and reading and its sensitivity. Two hundred children were studied for the comparative merits of each tuberculin: 100 with Koch's old tuberculin, in dilutions of 1:5,000, 1:1,000, 1:100 and 1:10; 40 with Koch's old tuberculin, esotuberculin of Finzi and purified protein derivative, and 50 with Koch's old tuberculin and the purified protein derivative.

In all the tests the same technic prevailed: dry sterilized syringes and special needles of small caliber and short bevel were used; the skin was disinfected with alcohol and then allowed to dry; a control test was read in forty-eight hours, and a thorough examination was made of local, focal, organic and general reactions.

The reading was made in the following manner: 1 plus for each area of reaction between 5 and 10 mm. in diameter; 2 plus for each area of reaction between 10 and 20 mm. in diameter; 3 plus for each area of reaction more than 20 mm. in diameter, and 4 plus for each reaction that was accompanied by a bleb and necrosis.

We found that the sensitivity of Koch's old tuberculin, that of esotuberculin of Finzi and that of the purified protein derivative are much alike in the whole range of such dilutions as 1:5,000, 1:1,000, 1:100 and 1:10.

We advise the use of purified protein derivative and esotuberculin of Finzi for tuberculosis surveys on a large scale because of their uniform results. For daily practice we prefer Koch's old tuberculin in dilutions of from 1:10,000 to 1:10, making the reading from forty-eight to seventy-two hours later. Purified protein derivative and the esotuberculin of Finzi produce little erythematous reaction and are consequently suitable for the practicing physician, in that they reduce to a minimum the error of interpreting as a positive reaction a simple erythematous reaction.

Pathologic Bioclinical Diagnosis of Tuberculosis in Infancy. Dr. Fausto C. Tucci, Buenos Aires.

Today experience permits one to discard the opinion, held for a long time, that tuberculosis in the child, and especially in the young infant, has an outcome almost always fatal.

The primary infection of the nursling and the very young child is frequently controlled and overcome, so that there is no cause for concern until, in many cases, obvious manifestations of the disease appear later. Because of this, systematic and early search for signs of the disease constitutes the foundation stone of the antituberculosis structure.

The "plan of Klare" calls for systematized diagnostic investigation of tuberculosis in infancy and has for its basis the medicosocial inquiry, the diagnostic hunt for tuberculosis, the clinical examination and the roentgenographic exploration.

The fundamentals on which the pathologic, bioclinical diagnosis rests are: (1) epidemiologic study, (2) specialized clinical study, (3) tuberculin test, (4) roentgenographic study and (5) bacilloscopic study. Complementary examinations are (1) hematologic and biohumeral investigations, (2) all the common laboratory tests and (3) special tests.

The classification used for children examined in the Infant's Antituberculosis Dispensary is:

1. Children who are "not infected," their epidemiologic, biologic, clinical, roentgenographic and bacteriologic examinations all giving negative results. They are separated from the others.

2. Children "allergic" to tuberculin, further classified into: (*a*) children without bacillary morbidity but simply with positive reactions to tuberculin or "latent infection" and (*b*) children with manifestations of bacillary morbidity or those "sick with tuberculosis."

The first group of "allergic" children can be without an evident focus or with demonstrable thoracic, extrathoracic or mixed foci. The second group comprises, according to my interpretation, children with the following grades of disease: (1) attenuated tuberculosis, (2) active tuberculosis, (3) evolutional tuberculosis and (4) infective tuberculosis. These forms are also divided into closed and open tuberculosis.

Statistics for 1,448 children allergic to tuberculin were studied in my service and tabulated in accordance with the foregoing classification:

1. Latent infections		443
Without evident focus	44	
With evident focus	399	
(*a*) Thoracic focus	397	
(*b*) Extrathoracic focus	1	
(*c*) Mixed foci	1	
2. Attenuated tuberculosis		569
Without evident focus	21	
With evident focus	548	
(*a*) Thoracic focus	501	
(*b*) Extrathoracic focus	44	
(*c*) Mixed foci	3	
3. Active tuberculosis (325 closed, 62 open)		387
(1) Thoracic	321	
(2) Extrathoracic	22	
(3) Mixed	44	
4. Evolutional tuberculosis (11 closed, 30 open)		41
(1) Thoracic	39	
(2) Mixed	2	
5. Infective tuberculosis (5 closed, 3 open)		8
(1) Disseminated thoracic	3	
(2) Generalized (miliary)	5	

Erythrocyte Sedimentation Rate as an Index of Activity in Infantile Tuberculosis. DR. FAUSTO C. TUCCI and DR. EDUARD FONTAN, Buenos Aires.

Red cell and plasma factors that affected erythrosedimentation were studied. The following physiologic limits for the sedimentation rate were established: For the newborn infant without alimentation, 1 to 2 mm. per hour; for the newborn infant who has taken nourishment, up to 4 mm. per hour; for the child 2 to 6 years old, 3 to 7 mm. per hour; for the child 6 years or older, the same values as for an adult. For an adult, up to 4 mm. is normal, between 4 and 10 mm. can be physiologic or pathologic and above 10 mm. is pathologic.

Erythrosedimentation is accelerated in acute polyarticular rheumatism, inflammatory processes (of microbic, traumatic or parasitic origin), infectious diseases (scarlet fever, measles, typhoid, paratyphoid), suppurative bronchiectasis and in

tuberculosis and in persons with malignant tumors. It influences the diagnosis, prognosis and treatment of tuberculosis.

The erythrosedimentation rates in tuberculosis which we have established are: (*a*) in attenuated, thoracic forms, between 5 and 20 mm.; (*b*) in surgical tuberculosis with closed glandular, osseous or osteoarticular localization, between 10 and 30 mm.; (*c*) in active forms (simple, inflammatory, exudative processes and congestive processes with good prognosis), usually between 20 and 30 mm. but may be up to 80 mm.; (*d*) in progressive processes (primary tuberculosis, secondary and tertiary), between 40 and 120 mm.; (*e*) in the infective varieties, as (1) in the curable disseminated types (rates are approximate to those in attenuated and active tuberculosis), 20 to 30 mm., (2) in the caseous exudative types (rates coincide with those in the progressive forms), 40 to 120 mm., and (3) in generalized infections (acute miliary), not very elevated figures.

The normalization of the erythrocyte sedimentation rate is frequently the last index of the cure of tuberculosis.

In general, any treatment that does not improve the erythrosedimentation rate is ineffective. Pneumothorax is followed by a short period of improvement of the erythrosedimentation rate. The same occurs with other types of treatment, such as institution of hygienic and dietetic measures, phrenicectomy, thoracoplasty or chemotherapy.

Increase of the erythrosedimentation rate is not specific for tuberculosis. After eliminating the other causes that might accelerate it, a high erythrosedimentation rate necessitates making a careful search for tuberculosis. Once the diagnosis of tuberculosis is made, a high figure indicates with some exactness the severity of the infection. The curve of the erythrosedimentation rates is an index of the modifications imposed on the disease by the treatment.

Bacilloscopic Examination of the Sputum and Gastric Contents: Application of the Thick Drop Method. Dr. Fausto C. Tucci and Dr. Jose B. Gomez, Buenos Aires.

We wish to point out the importance of gastric washing and its simple technic. Armand-Delille and Vibert, the enthusiasts for the method, found the tubercle bacillus in 100 per cent of 700 children with caseous, ulcerated tuberculosis and in 50 per cent of those whose roentgenographic picture was suggestive. Opitz in 1933 obtained positive results in 107 of 206 children with various forms of tuberculosis and 21 carriers of nonspecific pulmonary disease.

Acuña examined the gastric contents of 111 persons. By inoculation of the material not treated with 5 per cent sulfuric acid into guinea pigs he obtained 33 positive results, or 29.7 per cent; by inoculation of the material treated with sulfuric acid, 25 positive results, or 22.5 per cent; by means of culture, 16 positive results, or 14.4 per cent, and 2 positive results, or 1.8 per cent, by means of bacilloscopic examination.

Difficulties are found in practice in making the inoculations, and excessive time is often required for reinoculations. We have utilized a more simple, rapid and economical procedure which has the name of the "thick drop" method.

Results with this procedure may be compared with those obtained with inoculation or culture. Nevertheless, the method is ineffective in fixing the individuality and enabling the recognition of the acid-resistant bacillus found in the examined material. Neither does isolated bacilloscopic examination allow differentiation of the tubercle bacillus from the paratuberculous varieties, such as those of smegma, wax, butter and milk. Acid-resistant, nontuberculous bacilli are exceedingly rare in the mucous or mucopurulent secretions of the respiratory tract; this fact induced one of us (Tucci) to add to the examination of the sputum the "thick drop" procedure.

Five per cent of the acid-resistant bacilli found in the gastric contents, in the investigations made during 1939 in the department of tuberculous pathology and

medical tuberculosis, were not pathogenic and were therefore considered paratuberculous. In these instances only inoculation in the guinea pig effected their individualization.

In spite of the inconveniences noted, we believe that the thick drop procedure has its value as a means of rapid investigation of the bacillus.

Medical Treatment of Tuberculosis of Childhood. Dr. Pedro Depetris, Córdoba.

There are several different specific forms of treatment for the tuberculosis of childhood, such as, serum, vaccine and protein therapy, the use of tuberculin and chemotherapy. Serum therapy has failed to be of benefit. Recently, however, Jousset has brought forward a serum of which he is very hopeful. Efforts toward active immunization have been myriad, and the number of vaccines is innumerable, but the occasional successful attempt has been offset by indifferent or frankly harmful reactions in other instances, a fact that has caused this form of treatment to be abandoned in pediatrics. However, a short time ago, Grasset, by employing simply a formaldehydized tuberculosis endotoxoid or one made from horse serum immunized by toxoid and the products of lysis of live bacilli, obtained satisfactory results in juvenile and adult tuberculosis, which are well worth mentioning.

Tuberculin therapy has its fervent adherents; others consider it a therapeutic error, especially for the nursling.

Chemotherapy consists of the use of coloring substances, rare metals and the salts of copper and gold. Gold therapy has its advocates and its antagonists.

Some mention should be made of such methods of physical therapy as heliotherapy, actinotherapy and radiotherapy.

It is still not known with certainty how the roentgen rays effect cures in some tuberculous processes, but the opinion is general that their effects are purely local. Their principal indications in the medical treatment of tuberculosis in the child are the following: (1) chronic tuberculosis of the bronchotracheal glands; (2) tuberculosis of the peripheral lymphatic glands, with the exception of lymphoma and caseopurulent lymphofibrogranuloma; (3) tuberculosis of the abdomen, and (4) cutaneous tuberculosis, for which the roentgen rays, at the present time, are the chosen therapeutic agent.

In regard to hygienic and dietetic measures, the fundamentals of the treatment for all types of tuberculosis and especially of the nonsurgical treatment for tuberculosis of the child, such plans as rest cure, fresh air cure and dietetic cure should be reviewed. The rest cure acts by diminishing muscular exercise, avoiding cardiac overactivity and pulmonary hyperventilation. The fresh air cure helps to strengthen the general defenses of the sick child to produce a progressive "toning-up" and to raise a bulwark against associated infections; furthermore, it places the lung in relative functional rest. The diet cure forms with the rest cure and the open air cure the three pillars of treatment. There does not exist any specific alimentary regimen.

Collapse therapy has reduced the mortality of infantile tuberculosis from 95 per cent to 50 per cent. Indications for its use are: (1) all forms of primary and postprimary tuberculosis with fusion of the pulmonary parenchyma (primary and secondary ulcerated infiltrations), (2) early infiltration, (3) caseous pneumonia, (4) severe and persistent hemoptysis and (5) laryngeal tuberculosis.

Pneumothorax can be performed unilaterally, bilaterally—simultaneously or successively—or contralaterally.

Contraindications for its use in the child are: extensive infiltrations of both lungs, noncollapsible lesions, pleural symphysis, serious dissemination or polyvisceral degeneration, severe cardiovascular disturbances, exophthalmic goiter and grave diabetes.

Phrenectomy and phrenic exeresis ordinarily are employed as a substitute for pneumothorax when it is not practicable to do the latter or when one wishes to

increase its efficiency. According to Brauer, thoracoplasty and apicolysis are contraindicated in young patients.

The following conclusions have been formulated:

1. Added infections (superinfections) should be avoided by isolation and by giving to all children with active lesions, in whatever period of the tuberculous cycle, the proper, adequate treatment, not abandoning it till the indications of cure so advise.

2. One should not place too much hope in the local cure but take care more especially of the general state of the child by placing him in the best possible condition of defense.

3. One should prolong medical vigilance over the residual lesions and even those completely cured, not only until there is readaptation but up to puberty itself.

4. Treatment of infantile tuberculosis, whether it is in the sanatorium or the home, should always be under the supervision of the pediatrician.

5. Finally, one should not forget that in antituberculous therapeutics no law is so valid as that of Arndt-Schultze which says, "Small doses excite; larger ones depress, and the largest ones kill."

Book Reviews

Kinderheilkunde—Lehrbuch für Ärtzte und Studenten. By Prof. Dr. Franz Hamburger and Prof. Dr. Richard Priesel. Price, paper, 24 marks, bound 26.40 marks. Pp. 606, with no illustrations. Vienna: Franz Deuticker, 1940.

This pediatric textbook in German has been written primarily for the general practitioner and makes no pretense of being as exhaustive as the average pediatric textbook. It aims particularly to describe the practical points and the management and treatment of the conditions depicted. Its style is different from that of any medical textbook in German I have ever read, in that it is sometimes almost conversational. There is not the usual joining of fact on fact to complete the consideration of any given subject. This approach is not reserved for the psychologic but is also used in the consideration of the common pediatric conditions.

The book has been divided into two main portions. The first consists of a general discussion of pathology, diagnosis and treatment with respect to the various systems of the body in childhood. The second is the discussion referring specifically to individual diseases.

Certain of the chapters are particularly attractive. The discussion of neuroses in childhood is handled in detail. The authors offer specific suggestions as to therapy based on the attack of underlying psychic traumas, the use of environmental change, suggestion by means of physical therapy or medication and, finally, reeducation of the parents and the child.

The discourse on epilepsy is focused on drug therapy and ketogenic diet. There is no mention of the use of electroencephalography either in the detection of epilepsy or in helping to determine its prognosis.

In the discussion of chorea, nirvanol (phenylethyl hydantoin) and arsenic are mentioned, but nothing is said of heat or vaccine therapy. The discussion of the differential diagnosis of chorea from other types of muscular disorders is well handled.

The subject of pneumonia is handled rather summarily from the standpoint of an American physician, in that the old classification of types I to IV is used. There is no comment on the use of serum therapy or of chemotherapy. The authors express content with their belief that pneumonia is almost never a fatal disease in childhood, particularly lobar pneumonia.

The authors advocate practical starvation and early lowering of the intake of fluid and salt for acute hemorrhagic nephritis. Paricularly are milk and certain other proteins interdicted. Few American clinicians agree with this point of view. The subject of pyuria is discussed in the usual adequate way.

The greatly discussed diarrhea and intestinal intoxication of infancy are handled most briefly, and parenteral administration of fluid receives inadequate consideration. Unless there is a special provision that general practitioners must not handle patients seriously ill of intestinal intoxication, I fail to see how the results can be favorable with the management outlined. I hope that the general practitioner will be sufficiently acute to remember the preface, which directs him to more detailed pediatric textbooks.

In the discussion of birth trauma, the importance of hemorrhage is thoroughly brought out, but nothing is said about asphyxia or anoxemia, which are of considerable current interest here.

At the end of the book there are chapters on poisoning in childhood, with advice on treatment. This portion of the book seems well organized.

Finally, there are chapters giving a number of favorite prescriptions in pediatrics. These satisfied a long felt curiosity on my part concerning current therapeutics on the Continent and did it most concisely.

On the whole, I believe that the authors have succeeded very well in their purpose to provide a text for general practitioners of their country. It should interest Americans, because it depicts a different point of view in an interesting and usually entertaining manner.

Chemotherapy and Serum Therapy of Pneumonia. By Frederick T. Lord, Elliott S. Robinson and Roderick Heffron. Price, $1.00. Pp. 174, with 9 illustrations and 12 tables. New York: The Commonwealth Fund, 1940.

This is the third in a series of handbooks published by the Commonwealth Fund and continues the review of progress in the knowledge of pneumonia. This series began with "Lobar Pneumonia and Serum Therapy," in 1936, and was continued in "Pneumonia and Serum Therapy," in 1938. The discoveries from the study of pneumonia have come so rapidly that these monographs are essential to keeping the medical profession informed about them. This monograph seems very successful in reviewing and correlating the published discoveries in this field. It is unquestionably up-to-date, many references being made to articles published early in 1940. While the authors admit that there has not been time for the accumulation of as much data as they would like, sulfapyridine having been used only since 1938, the data on serum-treated patients date from 1931. The apparent value and widespread demand for these types of treatment make dissemination of the newest knowledge valuable.

The monograph considers pneumonia in respect to its importance as a public health problem, its etiology, diagnosis and prognosis. The authors include a review of the knowledge of the inhibiting specific substances demonstrated by Cole to be formed by virulent pneumococcus and show the importance of this work in helping to judge the effectiveness of serum therapy.

Chemotherapy, in particular the use of sulfapyridine and its results, is then considered. This is followed by a review of information on serum therapy and a comparison of the two types of therapy. The chief conclusion reached is that both types of treatment under optimal circumstances decrease mortality. Sulfapyridine is capable of wider use because of its value in infections with all types of pneumococci. In certain instances the two types of therapy should be combined, especially in patients with bacteremia or with such complications as empyema.

The monograph points out the need of more careful diagnosis, especially in the matter of blood cultures, and of more thoughtful use of the serum in regard to dosage, and it demonstrates the need for wider use of the Francis skin test—the subcutaneous injection of a dilution of the specific soluble substance to determine adequacy of serum therapy by the appearance of a positive reaction.

The authors also point out the difficulty of the use of both types of therapy for children, the lack of data on a sufficient number of children with pneumonia and the difficulty of determining the specific organisms in pneumonia in childhood. They believe that with children the use of sulfapyridine is more practical than serum therapy.

The book is exceedingly well annotated, and careful footnotes give sources of information. The index is adequate, and the appendixes give information made available to physicians of Massachusetts by the board of health.

Child Psychology for Professional Workers. By Florence M. Teagarden, Ph.D. Price, $3.25. Pp. 641, with 8 illustrations and 11 tables. New York: Prentice-Hall, Inc., 1940.

This book was written for professional laymen—social workers, teachers, nurses and clinicians, who are professional workers in their own fields but laymen in other fields. For years the author has been engaged in clinical psychologic service for children and has taught child psychology. She now writes this textbook, which is designed to acquaint workers with normal children and to prepare them for understanding and helping abnormal children.

A social worker finds here a brief but lucid explanation of the principles of heredity against which he can check his knowledge of the subject. The chapter

on "The Child and His Home" includes a discussion on the "good" and the "bad" qualities of a home. This discussion would be helpful to a worker who had to decide whether a child should remain in his own home or be placed in a foster home. In spite of dire poverty and ill health, a home is still a "good" home if it furnishes the child the love and emotional security necessary. In the chapter on "The Child and His School" the author—herself a teacher—evaluates the past success of the school in meeting the needs of its pupils. One of the problems considered is truancy.

The author has compiled a bibliography that would be of assistance to a student. At the end of each chapter is a list of from forty-two to eighty-seven references, which are also incorporated into the body of the text. For instance, Dr. Teagarden gives her experience on the prevention and cure of fears in children and then gives five references for further reading. Again, she speaks of the effect on the pupil of the emotional state of the teacher and gives fourteen references. After a summary of the current thought on the effect of movies and radio on juvenile delinquency, she gives six additional references. There are six references for those interested in children with defective speech.

Diseases of the Digestive System and Food Allergy. By Josef S. Smul, M.D. Price, $3.50. Pp. 219, with no illustrations. New York: Medical Library Company, 1940.

The purpose of this book is to link diseases of the gastrointestinal system with food allergy. In the opening chapter the author states that some seventy hitherto separate diseases of the gastrointestinal system without known cause will be proved to be only different groups of symptoms of one disease, "food allergy," of the digestive organs.

The author is verbose, employing terminology much of which apparently has been coined for the occasion, and the book is confusing to the initiated as well as to the uninitiated. Most of the classification of gastrointestinal allergy as used in this volume is not to be found in any of the recognized textbooks on the subject.

There is little reference to the voluminous work in this field; in fact, the book gives only five or six references. No publication later than 1930 is referred to and one versed in the subject is aware that the most outstanding work in this field has been done within the past ten years. There is no bibliography.

There is much unnecessary repetition, particularly in respect to diets, which in themselves are not based on the experience of a well trained allergist or substantiated by reference to the literature. As an example, foods are divided into two main groups, "allergic" and "anallergic." The three most common foods to which clinical sensitivity is demonstrated, namely wheat, milk and eggs, appear in one form or another in both lists.

It is deplorable that a book of this nature should be foisted on the medical profession, as it gives an erroneous concept of a specialty which today is well grounded on scientific fact.

A Manual of the Common Contagious Diseases. By Philip M. Stimson, M.D. Third edition. Price, $4.00. Pp. 465, with 54 illustrations and 6 plates. Philadelphia: Lea and Febiger, 1940.

There is no book in the field comparable to Stimson's "Manual of the Common Contagious Diseases."

In the third edition measles, scarlet fever, chickenpox and smallpox are illustrated by nine photographs in color which are of unusual excellence in details. A brief discussion of the virus diseases is another new feature, and all subject matter has been revised to date.

Chapters on "Principles of Contagion," "Serum Reactions" and "General Management of Contagious Diseases," which are of particular value, have held an important place in previous editions.

A glossary provides a convenient means of ready reference to a variety of terms commonly employed in connection with contagious diseases.

This book is admirably written, and the profusion of illustrations and tables adds to its worth. A bibliography at the close of each chapter will prove useful.

The author is entitled to the utmost praise for accomplishing even more in this edition than in the former editions of his work.

A Comparative Study of the Seasonal Incidence of Mortality in England and Wales and in the United States of America. By E. Lewis-Faning. Price, 1s. net. Pp. 69, with 13 illustrations and 17 tables. London: His Majesty's Stationery Office, 1940.

This is one of the Medical Research Council's special report series and is an attempt to compare mortality in England, Wales and the United States as to seasons. The author states that the study was limited to the use of official data and to a consideration of the large group of "unspecified causes" of death. However, it is without doubt the best study published to date in such compact form.

The conclusions are that the mortality during the winter in England and Wales is higher than in the United States, but the mortality in summer is lower. The more frequent causes of death during the winter period in England are the respiratory disturbances, including pneumonia and tuberculosis. It is an interesting fact that the more favorable balance of mortality for England and Wales for the summer months over the United States is due to less cardiac disease and fewer violent deaths.

Modern Diabetic Care. By Herbert Pollack, M.D. Price, $2.00. Pp. 216, with 13 illustrations. New York: Harcourt, Brace and Company, 1940.

This book is written as though the author were talking to a small group of physicians, patients and dietitians with a special interest in diabetes mellitus. The development of the knowledge of diabetes is presented in an easy and interesting fashion. Then the discussion proceeds to normal nutritional requirements and the use of various types of insulin in aiding the diabetic person to meet these requirements. Emergencies and complications and surgical operations for the diabetic subject are next discussed.

The chapters on diabetes in childhood and adolescence and pregnancy in diabetic women are brief, and one could wish that the author had given greater consideration to these subjects.

The last chapters are concerned with laboratory tests, planning of diets and tables of food equivalents and substitutions.

The ease and simplicity of presentation are such as must come from a thorough understanding of the subject. The book can be highly recommended to all interested in diabetic problems.

Reports on Medical Progress, 1939. Compiled and edited by Dr. Robert N. Nye. Price, $5.00. Pp. 562, with no illustrations. Boston: Little, Brown and Company, 1940.

During 1939, the *New England Journal of Medicine* ran a series of articles covering recent progress in the various specialties and in other interesting aspects of medical knowlege. This books consists of a collection of these articles. The fifty-four authors were carefully chosen, and the sound background of each is evident in the presentation of his subject. Each contributes from his knowledge the important developments in the field considered. Such a review is probably far more valuable than an attempt to cite every contribution to the literature, and it certainly provides much more interesting reading. Both the specialist and the general practitioner may find here practical help in diagnosis and treatment, as well as new facts to add to his fundamental knowledge.

Précis d'alimentation des nourrissons. By Eugène Terrien. Price, paper, $0.80. Pp. 308, with 8 plates, many tables. Paris: Masson et Cie, 1939.

This book is on infant feeding. The feeding of the child is outlined for the first year, and various artificial feedings are discussed, although most stress is placed on breast feeding for the first six months. The last part of the book is devoted to different methods of feeding to combat the digestive disturbances of infancy and many chronic conditions. This is a good practical book in French.

Directory of Medical Specialists, 1939. Dr. Paul Titus, Directing Editor. Price, $5.00. Pp. 1573, with no illustrations. New York: Columbia University Press, 1940.

In this book is a complete list of the licentiates of each of the various boards of specialties, together with rules governing the action of these boards. It is a very useful reference volume which, of course, must be renewed from year to year.

Common Procedures in the Practice of Paediatrics. By Alan Brown, M.D., and Frederick F. Tisdall, M.D. Third edition. Price, $5. Pp. 314, with 2 illustrations. Toronto: McClelland & Stewart, Ltd., 1939.

This text, enlarged and revised in the third edition, contains much to recommend it to the pediatrician and the general practitioner.

The section on infant feeding and on feeding older children—in fact, the work on dietetics in general—is excellent. There is a much needed chapter on behavior problems. On the whole, the text is adequate for the needs of the general practitioner or the pediatrician from a therapeutic standpoint.

Patologia del peritoneo en el lactante. By Dr. Ignacio Diaz Bobillo. Price not given. Pp. 186, with 21 illustrations. Buenos Aires: El Ateneo, 1939.

The author has adopted a rather unique scheme in this book on peritonitis in infancy. He devotes a chapter each to the primary causes of peritonitis, namely, appendicitis, pneumococcus, streptococcus, intestinal ulcers, gastric ulcers, diverticuli and tuberculosis. In these chapters the history, pathology, symptoms, diagnosis and treatment are fully discussed. At the end of each chapter are histories of illustrative cases. The work is readable, excellently illustrated and well done. There is a full bibliography on the subject.

Compendio practico de la alimentación del lactante. By Ernesto Gaing. Price, none given. Pp. 78, with 15 illustrations. Buenos Aires: El Ateneo, 1940.

This book is a short résumé in Spanish of the principles of infant feeding. Considerable space is given to breast feeding and its technic. A cow's milk formula is advised if artificial feeding is necessary. The more common disturbances of artificially fed infants are discussed and suggestions for their treatment are given. This practical and readable little book is illustrated with graphs and drawings.

The Chemical Composition of Foods. By R. A. McCance and E. M. Widdowson. Price, $2.50. Pp. 150, with no illustrations. New York: Chemical Publishing Company, Inc., 1940.

This book contains exhaustive studies not only on fresh but on cooked foods, the recipes for cooking being given. The results of this work vary in some details from those of former examinations. The whole forms an extremely valuable reference book.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, University of Michigan, Ann Arbor, Mich.

Canadian Committee:

Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston, Mass. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandsche Vereeniging voor Kindergeneeskunde

President: Prof. Dr. J. van Lookeren Campagne, Hofstraat 16, Gröningen, Holland.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340, 's Gravenhage, Holland.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

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*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jorge Muñoz Turnbull, Av. Alvaro Obregón 186, Mexico, D. F.
Secretary: Dr. Fernando López Clares, Medellín 191, Mexico, D. F.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Conrado Pelfort, Av. 18 de Julio 1246, Montevideo.
Secretary: Dr. Héctor Mourigan, Av. 18 de Julio 2175, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Julius H. Hess, 104 S. Michigan Ave., Chicago.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. J. B. Bilderback, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel Peabody, Memphis, Tenn. Time: Nov. 18-20, 1940.
Region I. Place: New Haven, Conn. Time: March 27-29, 1941.
Region II. Place: Richmond, Va.
Region III. Place: Palmer House, Chicago. Time: May 15-17, 1941.
Region IV. Place: Fairmont Hotel, San Francisco. Time: May 1-3, 1941.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Dr. D. L. Richardson, 593 Eddy St., Providence, R. I.
Secretary: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.

American Pediatric Society

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Place: Hot Springs, Va. Time: May 22-24, 1941.

Canadian Society for the Study of Diseases of Children

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. A. Ashley Weech, 3975 Broadway, New York.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. S. G. Henricke, 4215 N. E. Hancock St., Portland, Ore.
Secretary: Dr. J. S. Backstrand, 333 Wyatt Court, Salem, Ore.

Rocky Mountain Pediatric Society

President: Dr. Donn Barber, 802½–8th Ave., Greeley, Colo.
Secretary: Dr. Kenneth Schmidt, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Harvey F. Garrison, 319 E. Capitol St., Jackson, Miss.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.
Place: Louisville Ky. Time: Nov. 12-15, 1940.

STATE

Alabama Pediatric Society

President: Dr. M. V. Adams, 803 Government St., Mobile.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. William Belford, 233 A St., San Diego.
Secretary: Dr. John J. Miller Jr., 2398 Sacramento St., San Francisco.
Place: Del Monte. Time: May 1941.

Florida State Pediatric Society

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. R. C. McGahee, 1345 Greene St., Augusta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. D. C. Darrow, 789 Howard Ave., New Haven.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Orville Barbour, 331 Fulton St., Peoria.
Secretary: Dr. Craig Butler, 715 Lake St., Oak Park.
Place: Chicago. Time: May 1941.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. H. Aubrey White, Alexandria.
Secretary-Treasurer: Dr. W. C. Rivenbark, 3503 Prytania St., New Orleans.
Place: Shreveport. Time: April 1941.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Secretary: Dr. William J. Orr, 135 Linwood Ave., Buffalo.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.
Secretary: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Place: Pittsburgh. Time: Sept. 29-Oct. 2, 1941.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Harry Towsley, University of Michigan Hospital, Ann Arbor.
Secretary: Dr. Leon DeVel, 110 E. Fulton, Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl. Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.
Place: Biloxi. Time: May 12, 1941.

Nebraska Pediatric Society

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Hampshire Pediatric Society

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

North Carolina Pediatric Society

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

Oklahoma State Pediatric Society

President: Dr. Ben H. Nicholson, 301 N.W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

South Carolina Pediatric Society

President: Dr. R. B. Josey, 1517 Hampton Ave., Columbia.
Secretary-Treasurer: Dr. Wilson Ball, South Carolina State Health Dept., Columbia.

Tennessee State Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Secretary: Dr. Gilbert Eblen, 611 W. Main Ave., Knoxville.

Texas Pediatric Society

President: Dr. C. P. Jasperson, 509 Nixon Bldg., Corpus Christi.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Fort Worth. Time: May 14, 1941.

Virginia Pediatric Society

President: Dr. John M. Bishop, 511 Medical Arts Bldg., Roanoke.
Secretary: Dr. E. H. Harper, 301 Rivermont Ave., Virginia Beach.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Raymond Sloan, 1139–4th Ave., Huntington.
Secretary: Dr. Thomas G. Folsom, 1139–4th Ave., Huntington.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Secretary: Dr. David Zahn, 2474 Valentine Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Archibald Smith, Garden City, N. Y.
Secretary: Dr. Walter Coles, 604–2d St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Tuesday of April and September.

Chicago Pediatric Society

President: Dr. Philip Rosenblum, 2376 E. 71st St., Chicago.
Secretary: Dr. Bengt Hamilton, 826 E. 61st St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Edgar Loomis, 351 W. Jefferson Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Robert J. Mason, 460 Birmingham Rd., Birmingham, Mich.
Secretary: Dr. J. Hugh Lewis, 2966 Biddle Ave., Wyandotte, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Stephen C. Redd, 157 Forrest Ave. N. E., Atlanta.
Secretary: Dr. C. Dixon Fowler, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Thomas J. Donovan, 3820 Fannin St., Houston, Texas.
Secretary: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. John Aull, 1103 Grand Ave., Kansas City.
Secretary: Dr. George Herrman, 1107 Bryant Bldg., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Alonzo Cass, 1908 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Gladys Patric Shahovitch, 3936 Roderick Rd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sydney Nussbaum, 247 Ocean View Ave., Brooklyn.
Secretary: Dr. Harry Bikoff, 850 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. A. A. Trivilino, 88-07–150th St., Jamaica, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Ong, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. William F. Burdick, 5402 Connecticut Ave. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. S. F. Morgan, 2577 N. Downer Ave., Milwaukee.
Secretary-Treasurer: Dr. F. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Leslie O. Ashton, 850 Park Ave., New York.
Secretary: Dr. Alfred Langmann, 108 E. 68th St., New York.
Place: New York Academy of Medicine, 2 E. 103 St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roland E. Nutting, 205 W. 2d St., Duluth, Minn.
Secretary-Treasurer: Dr. John M. Adams, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. J. Byron Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Friday of each alternate month.

Philadelphia Pediatric Society

President: Dr. Pascal F. Lucchesi, 4000 N. Front St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. E. L. Piper, 3200–5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Charles L. Outland, 312 N. 9th St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. W. L. Bradford, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: First Friday of each month from October to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Donald C. Shelby, 3780 Wilshire Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Mark Osterlin, Central Michigan Children's Clinic, Traverse City, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Time: Nov. 15-16, 1940.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. M. Bernard Brahdy, 531 E. Lincoln Ave., Mount Vernon.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Ave., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.